

NASA Contractor Report 3922(31)

## USSR Space Life Sciences Digest

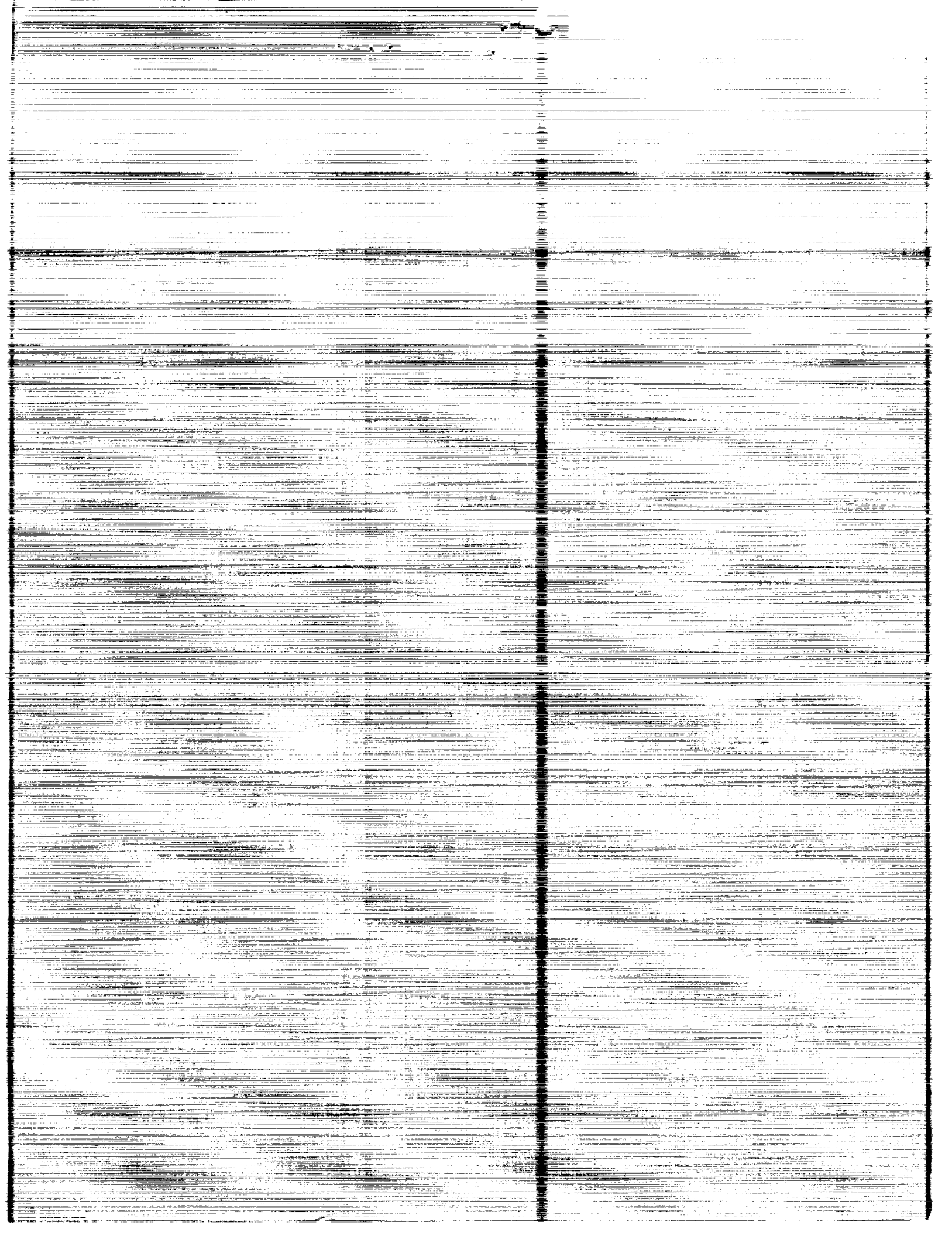
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# USSR Space Life Sciences Digest

## *Issue 26*

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<i>Reader Feedback Form</i>	v
<i>From the Editors</i>	vi
<b>BIOLOGICAL RHYTHMS</b>	1
The problem of desynchronization in space flight.	1
A raster-method for analyzing the periodic structure of biological rhythms.	2
Biological Rhythms In Space Biology and Medicine	4
<b>BODY FLUIDS</b>	6
Body fluid status during a 120-day period of hypokinesia with head-down tilt.	6
<b>CARDIOVASCULAR AND RESPIRATORY SYSTEMS</b>	8
Tolerance for provocative tests under conditions of a 1-year exposure to hypokinesia with head-down tilt.	8
A study of orthostatic tolerance and status of central and peripheral hemodynamics in hypertensive subjects undergoing a 7-day period of "dry" immersion.	10
Functional and metabolic changes in the heart during adaptation to high-altitude hypoxia.	11
Cardiac contractility in rats after chronic stress and thyroid.	13
Ca <sup>2+</sup> reactivity of ventricular actomyosin in rats exposed to gravitational loading.	14
<b>ENZYMOLGY</b>	15
Changes in activity of mitochondrial oxidative enzymes in skeletal muscles of rats during the recovery period after hypokinesia varying in duration.	15
Neutral peptide hydrolases in the blood serum and lungs under conditions of hypoxia.	16
<b>EXO BIOLOGY</b>	18
Simulation of abiogenic thermal polycondensation of amino acids in the Earth's lithosphere in areas of intense volcanic activity.	18
The Biological Effects of Lunar Soil	20
<b>HISTOLOGY</b>	24
Reactions of skin basophils of rats to exogenous hypoxia: A study of certain correlations.	24
<b>HUMAN PERFORMANCE</b>	25
Psychophysical characteristics of sensorimotor performance of an operator after short-term exposure to simulated hypogravity.	25
Diurnal variations in the efficiency of operator mental performance in shift work.	27
Apparatus and Methods for Investigating Operator Performance	28
<b>LIFE SUPPORT SYSTEMS</b>	30
Growth and development of one-celled algae as a component of an "algobacterial cenosis - fish" ecosystem under space flight conditions	30
Investigation of the growth and development of chlorella exposed to space on COSMOS-1887.	32
The formation of a wheat microbial cenosis on a manned space flight.	34
Matter balance during the catalytic oxidation of water mixtures by hydrogen peroxide.	36
<b>METABOLISM</b>	38
Serum proteins and products of nitrogen metabolism in humans undergoing long-term hypokinesia.	38
Activation of glycolysis, decreased glycogen reserves and lack of glucocorticoid control of enzymes of carbohydrate metabolism in the liver of rats undergoing long-term hypokinetic stress.	42
<b>MICROBIOLOGY</b>	44
Weightlessness and Elementary Biological Processes	44
<b>MUSCULOSKELETAL SYSTEM</b>	48
Mineral density of skeletal bones in humans exposed to simulated microgravity.	48
Changes in the periodontium in long-term hypodynamia and the use of diphosphonates and silatran to prevent these changes.	50
The Skeletal System and Weightlessness	51

<b>NEUROPHYSIOLOGY</b>	53
Characteristics of nocturnal sleep in monkeys on the ground and during space flight on COSMOS-1667.	53
A study of the structure of the receptor organs of the vestibular apparatus in rats after flight on COSMOS-1667.	55
Study of the pathogenesis of the neurological form of decompression sickness in rabbits.	58
Change in reflexive vestibular activity in response to orthostatic loading.	59
<b>NUTRITION</b>	60
The effect of increased consumption of vegetable protein on calcium metabolism in rats undergoing hypokinesia.	60
Thiamin metabolism in rats with a B1 deficiency exposed to hypokinesia.	62
<b>PERCEPTION</b>	63
Spatial orientation of pilots: Psychological Characteristics	63
<b>PSYCHOLOGY</b>	65
Psychological and Psychophysiological Adaptation in Humans	65
<b>RADIOBIOLOGY</b>	67
Acid tolerance of erythrocytes exposed to constant magnetic fields varying in rate of induction increase.	67
Certain biochemical mechanisms underlying the combined effects of extreme factors.	68
Possible mechanisms of the radiomodifying effect of exogenous hypoxia on microwave radiation.	70
The Biophysical Bases for the Effects of Cosmic Radiation and Radiation from Accelerators.	71
<b>SPACE BIOLOGY AND MEDICINE</b>	74
Biological experiments on COSMOS-1887.	74
370-Day antiorthostatic hypokinesia: Goals and research protocol	78
Report on: Twenty-first Symposium on Space Biology and Medicine	82
On the Pathogenesis of Weightlessness	86
<b>KEY WORD INDEX</b>	93

To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity of our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract Number	Incorrect or inappropriate term	Suggested rendering

**v**

## FROM THE EDITORS

This is Issue 26 of the USSR Space Life Sciences Digest. Starting with this issue, editor Lydia Hooke will be using her married name of Stone. Of particular interest in this issue are the conclusions of Soviet books on the biological effects of Lunar Soil (page 18) and the effects of weightlessness on elementary biological processes (page 44), a review of biological experiments performed on biosatellite COSMOS-1887 (page 74), and an article on the pathogenesis of weightlessness (page 86). Three articles on CELSS are abstracted in the Life Support Systems section, starting on page 30. A conference of the Intercosmos nations on Space Biology and Medicine is reviewed starting on page 82.

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## BIOLOGICAL RHYTHMS

### PAPERS:

P1193(26/90) Alyakrinskiy -BS.

***The problem of desynchronization in space flight.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5):4-8; 1989.

[33 references; 5 in English]

Biological Rhythms, Desynchronization; Circadian Rhythms, Work Schedules

Humans, Cosmonauts, Animals

Space Flight; Adaptation Syndrome

Abstract: The author discusses rhythm as a fundamental attribute of all living systems. Rhythms with a circadian period are considered central since they parallel the dynamics of the two basic states of animals -- sleep and waking. Only work schedules that take circadian rhythms into account will support optimal performance. Coordination of circadian rhythms is an essential prerequisite for physiological well-being. Circadian rhythms are considered an evolutionarily reinforced mechanism for supporting homeostasis. Their disruption is an obligatory early component of the alarm stage of the adaptation syndrome. Coordination (synchronosis) of biological rhythms is discussed in terms of dialectics, so that its opposite, desynchronization, becomes an integral part of the whole. A large number of examples are cited in which diseases or disorders of one system are accompanied by desynchronization of another system. For example, manic depressives display disruption of diurnal rhythm of catecholamine excretion. Desynchronization is a constant component of responses to stress factors of any sort.

American experiments on Biosatellite-3 revealed disruption of diurnal rhythms of blood pressure, body and brain temperature, pulse rate, and calcium excretion. The absence of similar changes in ground simulations suggests that weightlessness was a key factor. The author argues that in space flight the environment is full of desynchronizers, to a far greater extent than on Earth. This is why any disruption of sleep and waking, combined with the effects of other desynchronizers (particularly weightlessness) may decrease physiological tolerance. This suggests that regulating the daily schedule of cosmonauts is of critical importance.

Space chronobiology has formulated a number of important tenets: desynchronization as a necessary early component of the general adaptation syndrome; general biological laws of the circadian and cyclical nature of adaptive processes; the concept of circadian rhythm as a universal criterion of general physiological state; the concept of the cost of the daily cycle in terms of information and energy; and the development of functional "chronodiagnosis," the use of which increases the reliability with which individuals capable of successfully doing their jobs at any hour of the day can be identified. In examining the problem of shift work (a real possibility for long-term space flights) scientists have established the phenomenon of group synchronization.

## BIOLOGICAL RHYTHMS

P1187(26/89) Alpatov AM.

***A raster-method for analyzing the periodic structure of biological rhythms.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5):83-85; 1989.

[4 references; 1 in English]

Biological Rhythms, Periodic Structure

Theoretical Article

Mathematical Modeling, Raster Method

**Abstract:** The author proposes a "raster" method for analyzing biological rhythms. He asserts that the method is especially effective for investigating nonstationary multicomponent rhythms; for description of a highly changeable, noise-ridden pattern of fluctuations; and for rapid evaluation of the nature of processes the periodic structure of which is not known ahead of time. The method is extremely useful for examining free running circadian and ultradian rhythms in humans and animals "isolated from time cues." The method was validated over the course of 5 years using data on the biorhythms of insects, rats, monkeys, and humans.

The method involves the graphic identification of elements of repetition and regularity within a time series. The raw data are represented not in the form of a curve, but as a one-dimensional band, with the intensity of coloration at each point corresponding to the value on the ordinate, as is done on topographic maps to represent altitude. Distance along the band corresponds to the abscissa, i.e., the passage of time. Next the band is divided into segments of equal length, which are placed below one another like lines on a television screen (the source of the name "raster"). The pattern created will depend on the length of the segments. If the segment length corresponds to duration of a cycle, a pattern similar to depiction of a mountain range on a topographic map will emerge. If segment length is not close to the natural period of the time sequence, a pattern similar to noise on a television screen will result.

The author considers the advantages of this method to be its visual holistic representation and the completeness with which it represents complex dynamics of an oscillating process. Traditional methods, such as Fourier analysis, may be superior for accurately determining the exact period of the process.

# BIOLOGICAL RHYTHMS

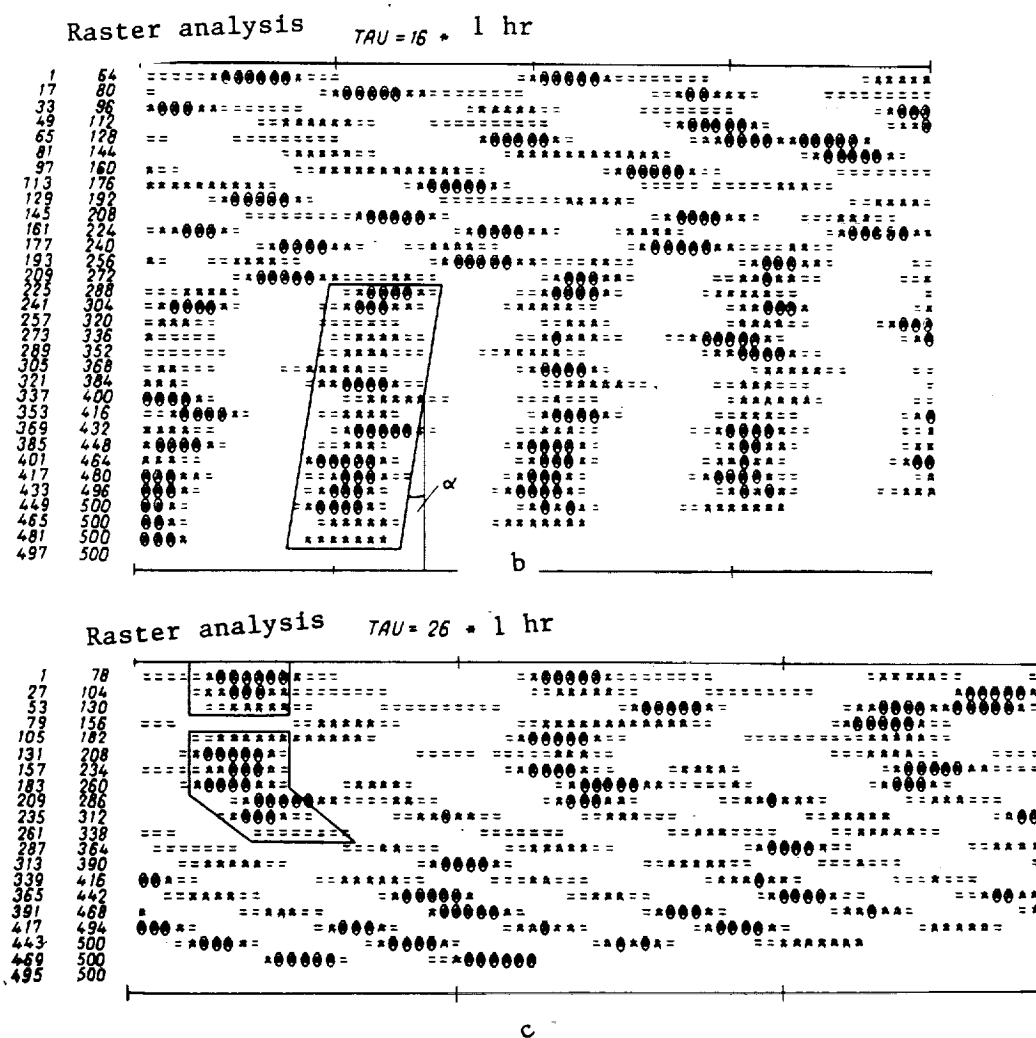
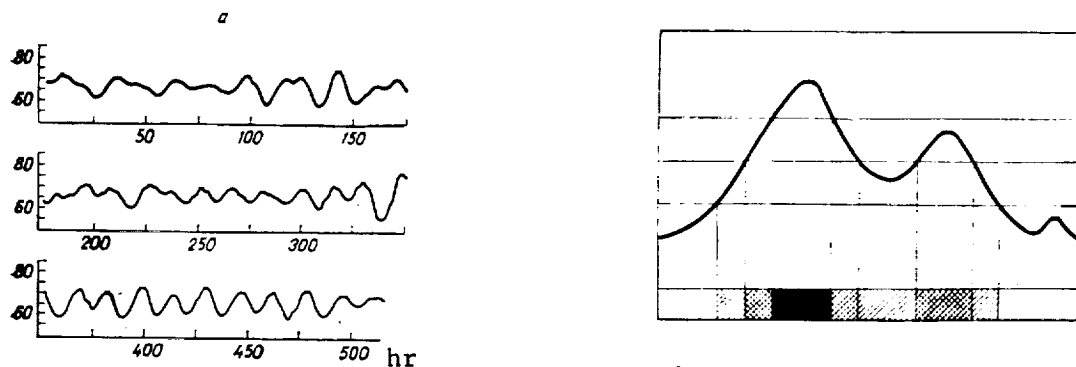


Figure 1: Diagram of representation of a curve in the form of a one-dimensional band

Figure 2: Example of the use of the raster-method. Representation of a free-flowing heart rate in a human isolated from time cues. Heart rate was measured every hour for a month

## MONOGRAPH:

M158(26/90) Gazonko OG, Editor.

Bioritmologicheskiye issledovaniya v kosmicheskoy biologii i meditsine

Биоритмологические исследования в космической биологии и медицине

**[*Biological Rhythms In Space Biology and Medicine*]**

Volume 64 In series: Problemy Kosmicheskoy Biologii,

Leningrad: Nauka; 1989.

[197 pages]

**KEY WORDS:** Biological Rhythms; Adaptation, Space Flight, Metabolism, Fat, Carbohydrates; Stress; Cardiovascular and Respiratory Systems; Human Performance, Shift Work, Endocrinology, Thyroid

**Annotation:** This collection contains results obtained by scientists from the USSR, Mongolia, GDR, Czechoslovakia, and Poland. Data on the adaptation of animals to space flight and on periodic physiological processes obtained through research simulating space flight conditions are cited. It is demonstrated that changes occur in fat and carbohydrate metabolism and that diurnal rhythms are disrupted in animals and humans in a variety of stress situations. The book is intended for a wide range of biologists and physicians.

## CONTENTS

Introduction (5)

Alyarkrinskiy BS (USSR). The problem of circadian rhythms (12)

Stepanova SI (USSR). Diurnal rhythms of parameters of the human cardiorespiratory system (34)

Shchukin AI (USSR). Chronobiological aspects of the problem of two-shift work (61)

Lkhagva L (Mongolia). Diurnal rhythm in human body temperature under conditions of horizontal hypokinesia (76)

Gumenyuk VS (USSR). Temporal patterns of mental productivity under conditions of a relatively free daily schedule (83)

Galichiy VA (USSR). Periodic processes in the human external respiration system in response to passive upright position (94)

Hecht K, Wachtel E (GDR). The interrelationship between circadian and minute rhythms in Wistar rats after space flight on COSMOS-1129 (124)

Hecht K, Wachtel E, Drescher U, Yevgenov K (GDR), Il'yin YeA, Korol'kov VI, Shlyk GG, Poshekhonov OF (USSR). The effect of weightlessness on minute rhythms of sensory and motor functions in monkeys (141)

Alersova Ye, Alers I (Czechoslovakia). Oscillations in thyroid hormones in rats (147)

Alersova Ye, Alers I, Dyatelinka I, Shmayda B, Toropila M (Czechoslovakia). Diurnal dynamics of parameters of carbohydrate metabolism in tissues of rats after irradiation at various times of day (163)

## **BIOLOGICAL RHYTHMS**

Alers I, Alersova Ye I, Dyatelinka I, Shmayda B, Toropila M (Czechoslovakia). Circadian rhythms in concentration of lipids in bone marrow and thymus of rats: The effect of fasting, starting at various times of day (173)

Alers I, Alersova Ye I, Shmayda B, Toropila M, Dyatelinka I (Czechoslovakia). Multiday metabolic rhythms in rats (178)

Kwariiecky K, Klossowsky M (Poland). Physiological correlates of flight workload (184)

## PAPER:

P1180(26/90) \*Lobachik VI, Zhidkov VV, Abrosimov SV.

***Body fluid status during a 120-day period of hypokinesia with head-down tilt.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 57-61; 1989.

[6 references; none in English]

Body Fluids, Hydration, Extracellular Fluid; Metabolism, Mineral, Fats

Humans

Hypokinesia With Head-Down Tilt, Long-Term; Pharmacological Countermeasures, Physical Exercise, Ultraviolet Therapy

**Abstract:** This experiment investigated the status of body fluids in healthy humans undergoing adaptation to long-term hypokinesia with head-down tilt. Two experiments were conducted with identical magnitude and duration of head-down tilt (-5°, 120 days) and the same diet and water consumption conditions and experimental procedures. A total of 21 subjects participated. In the first experiment (n=6), no countermeasures were used. In the second, a total of 15 subjects were divided into 4 groups. Group 1 (n=3) used no countermeasures, repeating the conditions of the previous experiment. Their data were combined with those of subjects in the first experiment for purposes of data analysis. The 4 subjects in group 2 were given pharmacological countermeasures including drugs to prevent changes in mineral metabolism (xydiphon = hydroxyethylidene biphosphonic acid; and glukamak=??). to normalize lipid metabolism and pancreatic function (solizim, a lipolytic drug obtained from cultures of *Penicillium solitum* and F-99); and the hemopoietic stimulant, folicobalamin. This group also underwent a course of ultraviolet therapy. Group 3 (n=4) engaged in a program of physical exercise directed at preventing changes in the function of the musculoskeletal system. Group 4 received all countermeasures administered to groups 2 and 3. Total fluid volume in the body was measured through dilution of tritium oxide using a liquid scintillation counter. Volume of extracellular fluid was measured through dilution of stable bromine, the plasma concentration of which was measured using the X-ray fluorescent method. Circulating blood volume was measured using albumin labelled with <sup>131</sup>I. Volumes of intracellular fluid and interstitial fluid were computed. Measurements were made during a baseline period and on days 1, 60, and 120 of treatment. Six control subjects were studied on day 15 of recovery. To determine the state of total body weight (especially muscular) concentration of <sup>40</sup>K was measured during the baseline period, on day 120 of hypokinesia, and during the recovery period.

In the baseline period total body fluid for all subjects was within the physiological norms. Body fluid status was measured on day 1 of hypokinesia in all 15 subjects, who at this point had been treated identically. All subjects showed a decrease in extracellular fluid volume (in an amount averaging 2.2% of the baseline amount). These changes were attributable to a decrease in the vascular portion and a slight decrease in interstitial fluid. Changes in total and intracellular fluid were not significant. After 2 months of treatment, the control group displayed a more pronounced decrease in hydration. Body fluid volume had decreased to 94.2% of baseline, due exclusively to extracellular fluid which was at 88.3% of baseline level. Decrease in extracellular fluid was due primarily to a decrease in interstitial fluid, while circulating plasma volume was unchanged. On day 120 of treatment all control subjects displayed a tendency for further decrease in hydration, attributable to diminished extracellular fluid. Volume of intracellular fluid also dropped during the last half of treatment in control subjects.

Changes in the experimental groups were similar in nature to those in the control group; however some differences were noted. On day 60 of treatment hypohydration was 25-50% less

## BODY FLUIDS

extreme in the two groups participating in exercise than in the control group. In the drugs-only group (group 2) decrease in hydration was attributable to decrease in both interstitial fluid and in plasma; while in exercise groups the decrease resulted only from diminished interstitial fluid, with circulating plasma increasing. Total body fluid level normalized somewhat between days 60 and 120 in the drugs-only groups, while dropping slightly in the exercise and drug+exercise groups during this period. All groups also displayed a decrease in lean body mass and in concentration of  $^{40}\text{K}$  in the body. When 6 control subjects were studied on day 15 of readaptation all parameters were found to be normalizing.

The authors conclude that hypokinesia with head-down tilt causes generalized hypohydration with changes in extracellular fluid being most pronounced. The major changes occur by day 60 of treatment. However, between days 60-120 there was some tendency for changes to progress. Physical exercise had some normalizing effects on body fluids, but as duration of hypokinesia increased, the efficacy of this countermeasure diminished.

Table 1: Body fluids in subjects during treatment

Table 2: Body weight, its composition and concentration of  $^{40}\text{K}$  before and on day 120 of hypokinesia with head-down tilt

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

### PAPERS:

P1179(26/90)\* Mikhailov VM, Machinskiy GV, Buzulina VP, Geogriyevskiy VS, Nechayeva EN, Kryutchenko SG.

***Tolerance for provocative tests under conditions of a 1-year exposure to hypokinesia with head-down tilt.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 54-56; 1989.

[7 references; none in English]

Cardiovascular and Respiratory Systems, Orthostatic Intolerance, Aerobic Capacity

Humans, Males

Hypokinesia with Head-down Tilt, Prophylactic Countermeasures, Physical Exercise, Drugs, Anti-g Suit; Provocative Tests, Tilt, Exercise Loading

Abstract: In this study, 9 healthy male volunteers underwent a 370-day period of hypokinesia with head-down tilt ( $-4.5^\circ$ ). [NOTE: These may or may not be the same subjects or experiment as the other 370-day experiment described in this issue. There are discrepancies in the descriptions, e.g. angle of tilt.] Subjects were divided into two subgroups using different prophylactic countermeasures. Group A performed physical exercises similar to those performed on space station Mir; group B used an experimental set of countermeasures. [This article does not state that prophylactic measures were delayed for 120 days for group B. However, discussion in the text suggests that there was such a delay.] At various stages of treatment the exercise was supplemented with other countermeasures (lower body negative pressure /LBNP/, use of salt and fluid supplements, drugs, and use of bladderless anti-g suits). The results of tilt and exercise loading tests served as criteria for judging the effectiveness of countermeasures. The tilt test entailed bringing the subject into a vertical position ( $+75^\circ$ ) for 20 minutes. Maximal values of physiological parameters were recorded and used for comparison. Subjects also were given a graded exercise test on the bicycle ergometer in a supine position. Two exercise conditions were utilized: pedalling at a constant loading of 130 W and pedalling at a workload that varied with heart rate. During the first 4-5 minutes, work increased in steps until heart rate reached  $150 \pm 5$  beats/minute. Load was adjusted to maintain this heart rate for the next 3 minutes. A third test, of maximal aerobic capacity, involved walking in a vertical position on a treadmill at a rate of 5-6 km/hr with the treadmill's angle of tilt increasing every 3 minutes by 2.5% until the subject was exhausted and unable to continue. Throughout all three tests, heart rate, blood pressure, EKG (using tetrapolar chest lead), oxygen consumption and respiratory minute volume were recorded. Rebreathing of  $\text{CO}_2$  was used to determine circulatory minute volume. Amount of work performed, maximum oxygen consumption, and maximum aerobic power, and other physiological and ergometric parameters were recorded. The data obtained were processed using standard statistical programs.

Before treatment all the subjects tolerated the tests in a completely satisfactory manner, with physiological response corresponding to that of a normal, healthy person of the appropriate age. During hypokinesia the response of the cardiovascular system to upright position deteriorated in all subjects, but to a greater degree for subjects in group B. Four group B subjects experienced faintness, starting at day 60 of testing. Group A subjects did not feel faint. On day 360 of treatment response to the tilt test in all groups improved, evidently due to increased use of prophylactic measures. Use of the anti-g suit virtually completely normalized hemodynamic response to upright position. On day 128 of treatment subjects in group A did not differ significantly from baseline in their response to submaximal exercise. On day 248, there was an increase in maximal work performed, accompanied by an appropriate increase in  $\text{O}_2$



## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

consumption and respiratory minute volume and stable values of stroke volume. These results attest to high cardiorespiratory reserve potential. In group B, for whom countermeasures were not utilized during the first 120 days of hypokinesia, tolerance to submaximal exercise diminished. Total work performed decreased by 13%, and stroke volume values were very low. Subsequent to introduction of exercise on day 248, group B subjects showed some increase in work performed but the parameters of central hemodynamics were comparable to those on day 120.

Before treatment all subjects showed satisfactory response to the treadmill test. Exercise typically stopped due to muscular exhaustion; group differences were not significant. Exposure to hypokinesia decreased maximum aerobic power in both groups, but to a greater extent in group B. Not only did parameters deteriorate, but the test had to be stopped due to shortness of breath, frequently accompanied by vertigo and palpitation. Severity of these symptoms depended more on extent of cardiovascular deconditioning than on duration of treatment. A number of parameters of myocardial bioelectric activity were altered, and maximum oxygen consumption decreased. The greatest decrease in aerobic power occurred in group B on day 120 of treatment. During this test, subjects' oxygen consumption was 37.4% lower than before hypokinesia, with the comparable value for group A being 15.2%. When treadmill tests were conducted on subjects undergoing hypokinesia, signs of cardiovascular deconditioning included increased systolic and decreased diastolic blood pressure, decreased T-wave amplitude, disruptions of cardiac rhythm, and delayed recovery of parameters after exercise. These symptoms were more severe in group B. On day 360, group A subjects showed virtually no difference from baseline parameters, while parameters of group B subjects were a mean of 13% below baseline.

Table: Mean values of general hemodynamic parameters in response to upright position

Parameter Grp		Base-		Hypokinesia, days						Recov 63
		line	60	120	180	240	300	360	360+	
# episodes of faintness	A	- -	- -	- -	- -	- -	- -	- -	- -	- -
	B	- -	3	2	2	1	2	1	- -	- -
Heart rate per minute	A	84.3	133.5*	107.0*	125.8*	114.3*	117.8*	102.8*	76.0	92.5
	B	78.3	132.8*	133.6*	111.2*	120.2*	126.6*	98.8*	77.6	96.2
Increase in pulse/minute	A	21.3	61.3*	44.0*	54.0*	48.8*	43.5*	39.3*	17.8	27.0
	B	17.8	57.6*	58.0*	45.0*	52.0*	54.6*	36.2*	14.0	31.8*
Pulse pres- sure, mm Hg	A	23.3	18.5	16.7	14.5	16.5	22.3	18.5	16.7	18.8
	B	30.0	22.2	19.4	21.2	16.4	20.0	22.4	35.0	23.6

+ wearing anti-g suit; \* difference from baseline significant at  $p < 0.05$ .

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1181(260)\* Yevdokimova AG, Radzevich AE, Solovyeva FB, Vinokhodova TV, Mamayev VI, Belyayev SM, Ovchinnikova LK.

***A study of orthostatic tolerance and status of central and peripheral hemodynamics in hypertensive subjects undergoing a 7-day period of "dry" immersion.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 62-65; 1989.

[9 references; 2 in English]

Cardiovascular and Respiratory Systems, Hemodynamics, Central and Peripheral, Orthostatic Tolerance

Humans, Males, Patients, Hypertension

Immersion, Dry; Tilt Test

**Abstract:** A total of 11 male volunteers aged 45-55 suffering from primary hypertension participated in this 7-day study, which simulated weightlessness through the "dry" immersion treatment. Hemodynamic parameters were recorded on days 1, 2, 3, and 7 of immersion, in the readaptation period, and a number of times during a tilt test. Impedance plethysmography was performed on the whole body, head, upper and lower lobes of the right lung, right calf, and liver. The following parameters were considered: cardiac minute and stroke volumes, heart rate, power of the left ventricle, total peripheral vascular resistance, mean hemodynamic pressure, pulsed blood filling of the head, and upper and lower lobes of the right lung, liver, and calf. Linear blood flow rate was measured in the arteries of the calf, forearm, and carotid arteries at the same times as hemodynamic pressures. Tilt tests were performed before and after the immersion treatment, with orthostatic position being defined as an angle of 75° to the horizontal. The pre-treatment exposure to the position was 15 minutes. The post-treatment test was performed 15 minutes after termination of immersion and lasted 20 minutes. The following parameters were measured during the test: heart rate (from EKG), blood pressure, total peripheral resistance, minute and stroke volumes.

On the average, stroke volume decreased to 77% baseline during treatment and recovered (to 94%) during the readaptation period. Minute volume decreased to 77% during treatment and recovered completely after it. Mean hemodynamic pressure decreased to 84% baseline during treatment and recovered to 93% baseline in the recovery period. Total peripheral resistance increased insignificantly during treatment and recovered during readaptation. The power of the left ventricle decreased significantly (to 59% baseline) during treatment and recovered virtually completely at the end of a 3-day readaptation period. Blood flow in the head increased by 10% on day 3 of immersion and decreased sharply (to 70% baseline) during readaptation. The most pronounced changes occurred in the lungs, especially the upper lobes, where minute blood flow was 187% baseline during immersion. Effects persisted in diminished form during readaptation. Blood flow in the liver decreased by 32% baseline during treatment and recovered to 90% afterward. Blood flow in the calf decreased by 25% and recovered fully. Changes in linear blood flow were in the same direction as changes in central and peripheral hemodynamics. Linear blood flow rate increased in forearm arteries and decreased in leg arteries. Orthostatic tolerance was drastically reduced after treatment.

Table: Changes in linear blood flow rate in the arteries of the calf and forearm during "dry" immersion

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1182(26/90)\* Varosyan MA.

### ***Functional and metabolic changes in the heart during adaptation to high-altitude hypoxia.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 68-70; 1989.

[11 references; 3 in English]

Cardiovascular and Respiratory Systems, Cardiac Hypertrophy, Metabolism, Heart, Nucleic Acids

Rabbits

Adaptation, High Altitude Hypoxia

**Abstract:** This study was performed on 140 chinchilla rabbits at three altitudes: 1000, 2000, and 3250 m above sea level. Parameters were measured after 2, 7, 15, 30, or 60 days at these altitudes. EKGs were recorded from 12 standard leads. Hemodynamics were studied using the method of radioisotope cardiography with measurement of circulating blood volume, minute and stroke volumes, and coefficient of effective circulation. Myocardial tissue blood flow was assessed using clearance of  $\text{Na}^{131}\text{I}$ . Left and right hearts were weighed. Histological and histomorphometric analyses were performed on sections perpendicular to the long axis of the fibers. rRNA and tRNA in the left and right ventricle were isolated using phenol deproteinization. RNA concentrations were measured on the basis of absorption spectra. To evaluate the biosynthesis of different forms of RNA, sodium phosphate labelled with  $^{32}\text{P}$  was injected intravenously 2 hours before the animals were sacrificed. Data were analyzed using analysis of variance.

After short periods (2 and 7 days) of adaptation to hypoxia, hemodynamic stress was limited by the increase in circulating blood volume. During the transitional stage of adaptation circulating blood volume normalized. On day 2 minute volume increased at 2000 and 3250 m by 32 and 55% compared to control (1000 m) animals. Subsequently this parameter remained elevated although it decreased gradually. Initially increase in minute volume was attributable to increased heart rate, but during the subsequent period this increase was associated with increased contractile strength (i.e., high stroke volume). After 2 and 7 days at high altitudes, myocardial blood flow rate increased, to a greater extent at the higher of the two high altitudes. Data obtained confirmed that high altitude adaptation involves myocardial hypertrophy of both ventricles, with the stronger effect on the right. On day 15, the right ventricle had increased in weight by 40 and 80%, for 2000 and 3250 m, respectively. Corresponding values for the left ventricle were 10 and 42%.

Measurement of myocardial fibers on day 15 showed a thickening of the cross-sectional area in both ventricles, with a larger effect in the right ventricle. On the whole, hypertrophy of muscle fibers correlated with extent of hypoxia. EKG parameters followed an analogous pattern. Hemodynamic changes corresponded to those in electrical activity. The isotonic hyperfunction of the left ventricle led to moderate hypertrophy of the left ventricle, while the isometric hyperfunction of the right ventricle is associated with marked right ventricular hypertrophy. Values of EKG parameters were directly correlated with duration and extent of hypoxia exposure.

On day 7 of adaptation, concentrations of rRNA in the left ventricle were 7 and 22% greater than in control animals and 19 and 33% greater in the right ventricle for altitudes of 2000 and 3250 m, respectively. A similar pattern held for concentrations of tRNA. Radioactivity results were analogous. On day 30 of adaptation, there was some decrease in concentrations and radioactivity of ribonucleic acids compared to day 7, but values remained elevated compared to control. After 2 months of adaptation, no further changes had occurred in these parameters.

## **CARDIOVASCULAR AND RESPIRATORY SYSTEMS**

The authors conclude that during the process of adaptation to high altitude hypoxia, myocardial hypertrophy occurs as a result of activation of synthesis of nucleic acids.

Table: Change in concentration and biosynthesis of myocardial RNA during adaptation to high altitudes as a function of duration and extent of hypoxia

Figure: Changes in parameters of the circulatory system in rabbits during adaptation to high altitudes

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1186(26/90) Kuznetsov VI.

***Cardiac contractility in rats after chronic stress and thyroid.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 78-82; 1989.

[33 references; 8 in English]

Cardiovascular and Respiratory Systems, Cardiac Contractility

Rats, Female

Stress, Immobilization, Coarctation; Endocrinology, Thyroid Hormones

**Abstract:** This work addressed the tolerance of acute coarctation in the hearts of rats that had previously undergone chronic stress and investigated the possibility of correcting stress generated changes with thyroid hormones. Subjects were 25 white outbred female rats. Chronic stress was produced by placing 3-4 rats in a small cage in which normal activity and behavioral responses could not occur for a period of 2 months. Acute pressure was placed on the heart by narrowing the aorta in the subdiaphragm region. The animals were divided into 3 groups: group 1 was the control; group 2 animals were stress adapted and then subjected to 4 days of aortal coarctation; group 3 animals additionally received thyroid hormones in the form of "thyroidin" (desiccated, defatted thyroid of edible animals) in increasing doses, beginning with 1.5 mg per 100 g body weight up to 3 mg/100 g body weight, with the dose increasing by 0.5 mg/100 g every 4 days. Cardiac contractility was studied in anesthetized rats. Pressure in the cavity of the left ventricle was recorded electromagnetically using a mingograph??. To determine the maximum capacity of the myocardium, during the experiment the ascending aorta was constricted for 30 seconds and pressure was recorded during seconds 5 and 25 of treatment. The following parameters were determined from the pressure curve: heart rate, developed pressure in the ventricle, maximal rate of contraction and of relaxation of the myocardium of the left ventricle. The parameter of rate pressure product was computed as the product of heart rate and developed pressure, a contractility index was defined as the quotient of maximum contraction rate and developed pressure at the moment of maximum rate, index of relaxation was computed analogously, index of structural functioning was computed as the product of heart rate and developed power per unit myocardial dry weight. Data were tested statistically using Student's *t*.

Adaptation to chronic stress did not affect response of contractility parameters to 4 days of coarctation or to constriction at the fifth second of treatment. However, at second 25 of constriction, developed pressure decreased by 35%, maximal contraction and relaxation rates decreased by 28 and 25%, respectively. If parameters obtained at second 5 of treatment are compared, it would appear that in stress-adapted rats, maximum level of contractility is greater than in control rats, (as indicated by greater developed power, index of structural functioning, maximal relaxation rate, and contractile power). At second 25, both control and adapted animals displayed a depression of contractile function (compared to second 5), but to a much greater extent in adapted animals.

When thyroidin was administered, developed pressure and maximum contraction and relaxation rates increased in a state of rest, by 29, 32, and 41%, respectively. The maximal rate and index of relaxation also increased after 5 seconds of aortal constriction. At second 25 of this treatment, developed pressure, and maximal myocardial contraction and relaxation rate were greater than that of adapted animals not receiving thyroidin by 65, 85, and 85%, respectively, and did not differ from analogous parameters of control animals. Some parameters even exceeded those of controls.

**Table:** Effects of thyroid hormones on cardiac contractility of rats exposed to a 60-day period of chronic stress, in response to 4 days of resistance loading

## CARDIOVASCULAR AND RESPIRATORY SYSTEMS

P1190(26/90) Tikunov BA, Kayfadzhyan MA, Oganessian SS.

***Ca<sup>2+</sup> reactivity of ventricular actomyosin in rats exposed to gravitational loading.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 88-89; 1989.

[8 references; 3 in English]

Cardiovascular and Respiratory Systems, Ca<sup>2+</sup> Reactivity, Ventricular Actomyosin

Rats, Male

Hypergravity, Acceleration

**Abstract:** In this experiment male outbred rats were centrifuged at +5G<sub>x</sub>(increase gradient 1G min<sup>-1</sup>) for 25 minutes a day for 7 days. The first experimental group was injected with 0.2 ml distilled water, and a second experimental group with the Soviet drug obzidan (propranol hydrochloride) at a dose of 0.2 mg per 100 g body weight before treatment. A control group was maintained under vivarium conditions. A total of 120 animals were used. One day after the last rotation, animals were sacrificed. The concentrations of natural actomyosin and ATPases were measured in the myocardium, and kinetics of superprecipitation recorded.

Gravitational loading increased rate of superprecipitation of the actomyosin complex as well as activity of Mg<sup>2+</sup>-ATPase actomyosin. These increases were more pronounced in the left than in the right cardiac ventricle. Changes associated with hypergravity in group 3, receiving obzidan, were less pronounced. Hypergravity had an even greater effect on Ca<sup>2+</sup> reactivity of natural actomyosins. Rate of superprecipitation was increased by exposure to hypergravity, while activation of Mg<sup>2+</sup>-ATPase was decreased; changes were greater in the left ventricle. Obzidan normalized superprecipitation under hypergravity, but only tended to normalize Mg<sup>2+</sup>-ATPase activity.

The authors conclude that since cardioactive compounds have been shown to directly affect myofibril proteins, caution should be applied before they are used to correct transformation of genetic isoforms of myofibril proteins and to regulate their Ca-sensitivity.

Table 1: Rate of superprecipitation and Mg<sup>2+</sup>-ATPase activity of natural actomyosin in the cardiac ventricles of rats

Table 2: Relative activation of rate of superprecipitation and Mg<sup>2+</sup>-ATPase of cardiac ventricles of rats in the presence of CaCl<sub>2</sub>

## PAPERS:

P1182(26/90)\* Potapov PP.

***Changes in activity of mitochondrial oxidative enzymes in skeletal muscles of rats during the recovery period after hypokinesia varying in duration.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 65-67; 1989.

[12 references; 1 in English]

Enzymology, Oxidative Enzymes; Musculoskeletal System, Skeletal Muscles, Mitochondria  
Rats

Hypokinesia, Long- and Short-term, Recovery Period

**Abstract:** An experiment was performed on 164 white rats (of which 30 were treated as controls). Motor activity of experimental groups was limited through immobilization cages. Three hypokinesia durations were studied: 7, 15, and 30 days. A portion of the animals were sacrificed after each hypokinesia period and the remainder returned to vivarium conditions. During the recovery period, one animal from each group, including the control, was sacrificed daily.

Parameters were measured in skeletal muscle tissue of the anterior group of femur muscles. Mitochondrial fractions were separated out using differential centrifugation at 0-4°C. The mitochondria were solubilized. Activity of isocitrate dehydrogenase (ICDH) was estimated from rate of formation of reduced forms of pyridine nucleotides. Activity of pyruvate dehydrogenase (PDH),  $\alpha$ -ketoglutarate dehydrogenases (KGDH), and succinate dehydrogenases (SDH) was estimated from rates of increase of 2,6-dichlorophenolindophenol. Protein parameters were derived using Lowry's method.

Animals exposed to hypokinesia for 7 days displayed minimal changes. On day 7, activity of both forms of ICDH decreased, normalizing on days 4-5 of readaptation. After 15 days of limited movement ICDH activity also decreased. During readaptation the NADP-dependent enzyme recovered on day 7, while activity of NAD-dependent ICDH remained depressed until day 11 of readaptation. Activity of SDH and KGDH decreased appreciably during the initial portion of readaptation and remained depressed until the third week of the readaptation period. PDH activity dropped at the beginning of readaptation and then increased to above the norm from days 9-17.

The 30-day period of hypokinesia was associated with decreases in activity of all the enzymes. Activity of NADP-dependent ICDH returned to the norm on day 12 of readaptation and that of the other enzymes normalized during the third week of readaptation. The authors conclude that during the period of readaptation after hypokinesia, amino acids are used primarily for synthesis of contractile proteins and also of enzyme proteins that have critical significance for normalization of energy metabolism.

**Figure 1:** Changes in activity of oxidative enzymes in mitochondria of skeletal muscles in rats during the readaptation period after 7 days of hypokinesia

**Figure 2:** Changes of activity of oxidative enzymes in skeletal muscle mitochondria in rats during the readaptation period after 15 days of hypokinesia

**Figure 3:** Changes in activity of oxidative enzymes in skeletal muscle mitochondria in rats during the readaptation period after 30 days of hypokinesia

P1183(26/90)\* Ivashkevich AA, Nosar' VI, Kurbakov LA.

***Neutral peptide hydrolases in the blood serum and lungs under conditions of hypoxia.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 70-75; 1989.

[18 references; none in English]

Enzymology, Peptide Hydrolases, Blood Serum, Lungs, Proteolysis, Tissue Respiration  
Rats, Males

Cardiovascular and Respiratory System, Hypoxia; Adaptation, Barochamber Training

**Abstract:** This experiment had as its goal study of reactivity of neutral peptide hydrogenases of blood serum and the lungs and also investigation of the possible association of this reactivity with respiratory processes under conditions of hypoxia. Subjects were 64 outbred male rats of the same age and approximate weight. Oxygen consumption ( $VO_2$ ) was measured in a closed system with simultaneous recording of frequency and tidal volume, while subjects breathed air and then a hypoxic gas mixture containing 11%  $O_2$  for 10-15 minutes. Barochamber conditioning was begun with ascent to 3500 m. Every subsequent ascent was increased by 500 m to a maximum altitude of 7000 m. The animals spent 60 minutes at the target altitude, ascent and descent lasted 30 minutes each, and there was an interval of 90 minutes between successive ascents. A total of 15 ascents were performed at the rate of 3 per day. After the conditioning program was complete, respiratory parameters were again measured. Activity of neutral peptide hydrolases was investigated in blood serum and the lungs by an undescribed method. Enzymes were studied in conditioned and control animals decapitated after 15 minutes of breathing air or a hypoxic mixture ( $O_2=11\%$ ) under normobaric conditions.

The pattern of oxygen use before barochamber conditioning in response to a hypoxic test was not the same in all subjects. In some animals  $VO_2$  did not alter in response to the hypoxic medium, while in others this parameter decreased drastically; these animals were assigned to groups 1 and 2, respectively. Group 1 animals displayed lower respiratory minute volume and respiration rate while breathing air than did group 2 animals. While breathing air, animals of group 1 displayed higher activity of neutral peptide hydrolases in the lungs than animals of group 2. Respiration rate, tidal volume, and minute volume increased in both groups when the animals breathed the hypoxic mixture. Between group differences in activity of peptide hydrolases diminished when the animals breathed the hypoxic medium.

After barochamber conditioning, oxygen consumption while breathing air was the same in both groups. Differences in  $VO_2$  were noted only in minute 5 of breathing the hypoxic mixture. Respiration rate and tidal and minute volume increased in all animals breathing air as compared to pretraining conditions. After training, group 1 responded to the hypoxic mixture by an increase in tidal volume, while in group 2 minute respiration rate increased. Intergroup differences in activity of neutral peptide hydrolases when animals breathed air were even more pronounced than before training. When the hypoxic mixture was breathed, group 2 animals showed higher level of enzyme activity than group 1.

In blood serum, before barochamber training no intergroup differences were found in peptide hydrolase activity for either air or hypoxic mixture breathing. Nor were differences found after training when animals breathed air. However, after training, group 1 animals responded to the hypoxic medium with a pronounced decrease in enzyme activity in blood serum; group 2 animals showed no such reaction.

The authors conclude that their data confirm the close relationship between proteolytic processes and processes of tissue respiration, and suggest: 1) that a link exists between the



## ENZYMOLOGY

proteolytic activity of the lungs and their functional activity and 2) that neutral proteolases in blood may be a function of their level in the lungs. This in turn suggests a hypothesis that these enzymes participate in regulation of oxygen transport to the tissue by affecting the rheological characteristics of blood and vascular tonus. Not only does blood become saturated with oxygen in the lungs, but evidently there is also correction of the factors regulating oxygen transport to the tissues. The proteolytic system of blood, which serves as a trigger and mediator of blood coagulation, fibrinolysis, and the kinin, renin-angiotensin, and complement systems, not only protects the system from harm, but acts to maintain physiological homeostasis.

Figure 1: Changes in oxygen consumption while breathing air and hypoxic mixture

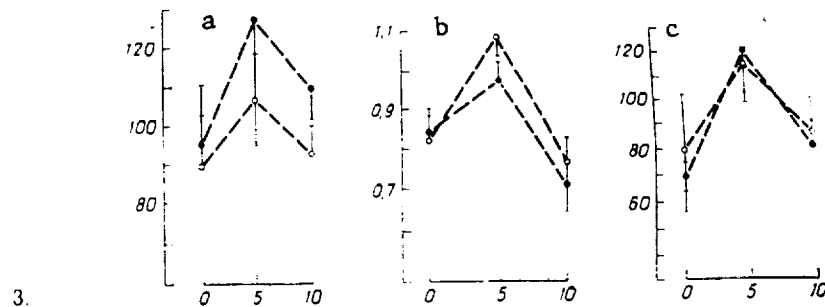
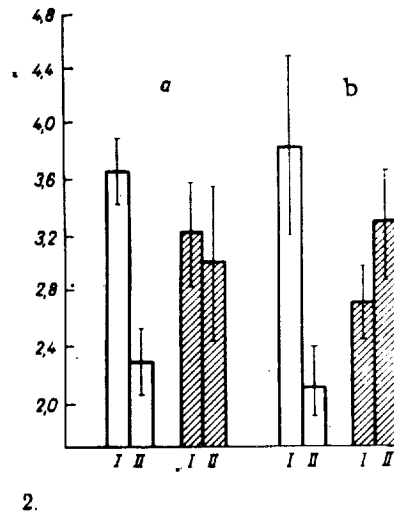


Figure 2: Change in activity (in mg/100 g) of neutral peptide hydrolases in the lungs in rats breathing a hypoxic gas mixture containing 11% O<sub>2</sub> in nitrogen

a - before, b - after barochamber training; I - group 1; II - group 2. White bars - air; hatched bars - hypoxic medium

Figure 3: change in respiratory parameters while breathing a hypoxic medium containing 11% O<sub>2</sub> in nitrogen

## PAPER:

P1194\*26/90) Larentyev GA, Rakitin LYu, Piskunova LA.

***Simulation of abiogenic thermal polycondensation of amino acids in the Earth's lithosphere in areas of intense volcanic activity.***

Zhurnal Evolyutsionnoy Biokhimii i Fiziologii

XXV(4): 417-423; 1989.

[13 references; 11 in English]

Authors' Affiliation: A.N. Bakh Institute of Biochemistry, USSR Academy of Sciences

Exobiology, Abiogenesis, Thermal Polycondensation

Amino Acids

Lithosphere, Simulation, Volcanic Activity

**Abstract:** The goal of this work was to perform abiogenic thermal synthesis of amino acid polycondensates under conditions that could have existed in the upper layers of the lithosphere of the primitive Earth in areas of active volcanic or heightened hydrothermal activity. Material included 0.01 M solutions of 1-amino acids: lysine, arginine, aspartic acid, glutaminic acid, glycine, alanine, isoleucine, phenylalanine, valine, leucines and the clay mineral kaolinite. Trypsin was utilized for the enzymatic hydrolysis of products of synthesis. The clay mineral was pulverized and organic contaminants removed. Then it was twice incubated with a solution of  $\text{MgClO}_4 \cdot 6\text{H}_2\text{O}$ ,  $\text{Zn}(\text{NO}_3)_2$ ,  $\text{F}_4\text{SO}_4 \cdot 7\text{H}_2\text{O}$  (at concentrations of  $2.5 \cdot 10^{-2}\%$ ) at  $\text{pH}=5.0$ , after which the thick suspension was poured into a pyrex tube. To improve the hydrodynamic properties of the reactor, layers of kaolinite were alternated with layers of tubes 2-3 mm (in diameter?). A solution of amino acid and salt in the aforementioned concentrations (6 ml) was added to the reactor. To prevent microbiological contamination, sodium azide was added to the reactor to a final concentration of 0.02%. At nitrogen pressure of (2-3  $\text{kg/cm}^2$ ) the solution was passed through the reactor, where the temperature was maintained at 40-45°. After the solution passed through the reactor, temperature in it was increased to 90°C. The contents of the reactor were desiccated by blowing nitrogen through it and they were heated again for 18-20 hours in relatively dehydrated state. Then the initial solution of amino acids (6 ml) was again added, the temperature decreased to 40°C and the operations repeated. There were 15 such cycles. The solution passing through the reactor and the alkaline (0.5 n  $\text{NH}_4\text{OH}$ ) extract from the reactor (eluate) were analyzed. The insoluble portion of the extracted material was separated using a filter with pores 2.5  $\mu\text{m}$  in diameter. After diafiltration, the fractions with molecular weight greater than 1000 were subjected to gelfiltration. The fractions corresponding to free volume (mol. weight >1500) were removed, boiled down and analyzed in a column on which the elution volume of blue dextran and insulin had previously been determined. The chromatographic fractions were submitted to optical chromatography. Hydrolysis of the products of synthesis was performed by? 6 n HCl in sealed, evacuated ampuls at 105°C for 24 hours. Analysis of the amino acids was conducted using a high pressure amino acid analyzer. In order to obtain infrared absorption spectra, solutions of the organic compounds were applied to plates. The solutions were dried and spectra recorded with a spectrophotometer. The concentration of metals in the chromatographic fractions was determined using an atomic absorption spectrophotometer. Hydrolysis of samples of trypsin was conducted in a 0.02 M solution of  $\text{NH}_4\text{HCO}_3$ ,  $\text{pH} = 8.1$  for 20 hours. A control condition was run to assess natural and laboratory pollution analogous to the main condition but without heating the reactor to 90°.

The eluate resulting from the procedure described above contained the initial amino acids (except phenylalanine) in quantities significantly exceeding those obtained in the control. In spite of the absence of serine in the initial mixture, this acid was present in the eluate in quantities which cannot be explained by contamination. Small quantities of cystine, threonine, tyrosine, histidine and proline found in the eluate are evidently contaminants. The eluate

contained large amounts of arginine, which the authors say they cannot interpret. Comparison of the amino acids in the polymer fraction of the portion of the solution passing through the reactor (breakthrough) and the eluate of the control experiment suggests that the kaolinite acts as a kind of filter on which contaminants accumulate as the amino acid solution passes through the reactor with the mineral. Infrared spectra of absorption ( $1550$  and  $1650\text{ cm}^{-1}$ ) and the positive biuret reaction attests to the presence of a peptide bond in the synthesized polycondensate. This is confirmed by the polymer's partial hydrolysis by trypsin. Analysis of the polymers obtained for metals showed that magnesium, iron, and zinc existed in the initial amino acid solution in a ratio by weight of  $1:2:3$  and in the polymer fraction of the products of abiogenic synthesis in ratio of  $2.5:1:1$ . This demonstrates the selectivity of the binding of metal ions in the process of thermal synthesis of peptide-like compounds. The fact that metal ions are components of abiogenically synthesized amino acid polymers is extremely interesting, since metals are important in various biochemical processes.

The authors conclude that not only could polymer molecules containing a peptide bond be derived from amino acids in the lithosphere through operation of a hydrothermal system, but they also could result from an infiltrational mechanism in the upper layers of the Earth's crust. In addition, metals such as iron, magnesium, and zinc, which are components of the active centers of modern enzymes, may enter into the structures of these polycondensates, possibly leading to some degree of "protoenzymatic" activity. When cooled in water-bearing layers? these polymers could have formed phase-separated systems where they could accumulate other abiogenically synthesized organic molecules.

Table 1: Amino acid composition of chromatographic fractions

Figure 1: Diagram of a device for modeling abiogenic polycondensation of amino acids in the Earth's lithosphere

Figure 2: Chromatogram of products of polycondensation of amino acids on a column

## MONOGRAPH

M156(26/90) Kustov VV, Belkin VI, Kruglikov GG.

**Biologicheskiye Effekty Lunnogo Grunta; Биологические Эффекты Лунного Грунта; [The Biological Effects of Lunar Soil]**

Volume 61 In series: Problemy Kosmicheskoy Biologii,

Leningrad: Nauka; 1989.

[103 pages; 47 references; 6 in English]

**Key Words:** Exobiology, Lunar Soil, Biological Effects, Fibrogenesis

**Annotation:** This book reviews the literature on the biological activity of lunar soil transported to Earth by American astronauts and also results of Soviet research and the authors' own experiments. These experiments assessed the biological effects of fine fractions of lunar soil obtained by Soviet rovers from the maria and highlands regions of the moon. Analysis of the material obtained supported the conclusion that none of the lunar soil samples studied were biologically inert. A working hypothesis concerning the possible mechanism underlying the pathogenic properties of lunar soil is formulated and experimentally confirmed.

## CONTENTS

Introduction (5)

Chapter 1: Review of the literature (7)

- 1.1 Research on the possible existence of the simplest life forms on the Moon (7)
- 1.2 Study of the effects of lunar soil on terrestrial microorganisms and fungi (9)
- 1.3 Study of the effects of lunar soil on animal tissue cultures and intact animals (10)

Chapter 2: Research on the biological effects on mammals of fine fractions of soil transported to Earth on the unmanned Luna-16 station (11)

- 2.1 Study of the biological effects of air passed through a specimen? of lunar soil (11)
- 2.2 Intraperitoneal administration of a supernatant liquid to animals
- 2.3 Introduction of a suspension of lunar soil into the gastrointestinal tract (14)

Chapter 3. Lunar conditions and their effects on the mineralogical composition and physical-chemical properties of lunar soil (14)

Chapter 4: Study of the biological activity of lunar soil from Mare Fecunditatis and its terrestrial analog introduced intratracheally (19)

- 4.1 Short description of the materials (19)
- 4.2 Biological investigations (21)
- 4.3 The effect of lunar soil on the structural and functional state of alveolar macrophages (35)
- 4.4 The effect of lunar soil on the formation of specific granulation tissue in the lungs of experimental animals (43)

Chapter 5: Study of the biological effects of lunar soil from the highland region of the Moon and its terrestrial analog introduced intratracheally (55)

- 5.1 Biological investigations (57)
- 5.2 The effect of lunar soil and its terrestrial analog on the structural and functional state of alveolar macrophages and the development of specific granulation tissue in the lungs of experimental animals (66)

## EXOBIOLOGY

Chapter 6: Comparison of the biological effects of lunar soil from the maria and highlands of the Moon (78)

Chapter 7: The mechanisms underlying the biological effects of lunar soil (84)

7.1 Research materials and methods (84)

7.2 The effects of the biological environment of an organism on lunar soil particles (87)

7.3 The effects of lunar soil particles on the cellular (cell-mediated?) reaction (92)

Conclusion (97)

References (100)

**Conclusion:** Having completed our presentation of the material relating to the biological effects of lunar soil and the etiology of its pathogenicity, we can draw certain general conclusions and formulate the most promising direction for further research on lunar material, as well as on other materials of extraterrestrial origin.

The research reviewed supports a conclusion that the specific conditions under which lunar soil formed, which are different from those accompanying formation of soil on Earth, created some degree of biological activity, as established by introducing samples into living organisms through various routes. This activity was most pronounced when soil samples were introduced intratracheally. In these cases, there was a slight general toxic effect of lunar material which was manifest in changes in certain integral hematological parameters and a whole series of biochemical indicators.

In addition, we noted moderately severe changes in pulmonary tissue: the development of pneumoconiosis of the cellular proliferative type with diffuse perivascular and peribronchial fibrosis, induced by the effect of phagocytosed? particles of lunar material on alveolar macrophages and pulmonary tissue. Here, lunar soil from the maria region (Luna-16) showed greater fibrogenic activity than soil from the highland region (Luna-20).

These differences in biological effects, in our opinion, may be due to the significant proportion of the particles composed mainly of aluminum silicate-rich anartzites in the highland sample, while the sample from the maria region contained a predominance of basalts, and also oxides varying in composition, as well as rock-forming, rare, and trace elements.

In addition, the fact that the samples from the maria region contained 3.1 times more finely dispersed particles of superparamagnetic iron than those from the highland region may be of some importance.

As the reactivity of the particles decreased over time, their effect on fibrogenic activity and also on a number of parameters of general toxicity decreased. To investigate this function, we derived a regression equation using an applied program package that paralleled the dynamics of

changes in parameters in the period after intratracheal introduction of lunar soil. Thus, for the parameters "pulmonary oxypoline" and "catalase index of the blood" these equations had the following forms:

for pulmonary oxypoline

$$y = -5.410 + 1.618x_1 + 1.743x_2 \quad (10)$$

(for soil from the mare region),

$$y = -.624 + 0.934x_1 + 0.62x_2 \quad (11)$$

(for soil from the highland region):

for the catalase index of blood

$$y = 0.912 + 0.43x_1 - 0.05x_2 \quad (12)$$

where  $x_1$  is the initial value of the parameters and,  $x_2$  is time in months.

All the equations are significant at a level of  $\alpha=0.01$ . The percentage of variance explained is 86% for equation (10), 99.7% for equation (11), and 98.6% for equation (12).

Value of the oxygen utilization parameter did not depend on initial parameter values (the sample consisted of  $n$  experimental animals). The variable  $x_2$ , exposure time in months, had a significant effect on the parameter, as evidenced by a reliable difference (sign test  $\alpha=0.01$ ) between values of oxygen consumption after months 3 and 6.

Body weight was a function of time after intratracheal introduction of soil obtained from the Mare Fecundatus (Luna-16).

$$y = 343.05 - 74.702 \cdot \frac{1}{x_2} \quad (13)$$

The percentage of variance explained was 90%. The equation is significant with a level of confidence of  $\alpha=0.01$ . Use of  $x_1$  (initial body weight) does not improve prediction of  $y$  compared to regression with  $x_2$ .

The functions obtained can be used to predict the possibility of change in these parameters over time in order to evaluate the pathogenic effect not only of lunar soil, but also of other extraterrestrial materials similar in physical and chemical characteristics or of formation conditions.

All this supports the hypothesis that the adverse physiological effects of lunar soil could be caused by the direct action of the particles themselves or of their surface, activated by the specific conditions under which they formed, as well as by aggressive compounds forming through contact of the lunar soil particles with body fluids. In a special experiment, we studied the effects of the biological medium on level of reactivity of lunar particles or their surface, and also the relationship between this parameter and magnitude of biological response. This experiment showed that the biological medium actively affects the physical/chemical properties of lunar material, while the latter, in turn, affect level of cytotoxicity.

Thus, during the first 60-80 days, due evidently to the effect of intensive hydrolytic processes, the surface activity of lunar soil particles decreased significantly, and they disintegrated or partially dissolved, possibly leading to migration of chemically active compounds of iron and

## EXOBIOLOGY

other elements into the biological medium. The particles themselves and these compounds had some effect on cellular elements. The magnitude of this effect for various particles was a direct function of the level of their surface activity, as estimated from the concentration of finely dispersed metallic iron.

Thus, the research performed supports the assertion that the tested samples of lunar soil from various regions of the lunar surface are not biologically inert and that the level of their biological activity is determined both by the physical and chemical properties of the lunar material itself, and by the reactivity of its surface.

The methods we used permitted only a preliminary evaluation of the danger associated with lunar soil. It goes without saying that in further investigations of lunar material, and also other materials of extraterrestrial origin, these methods must be augmented with other research techniques that could potentially reveal other biological effects of these materials and increase our understanding of the mechanisms through which they affect biological material.

## PAPER:

P1189(26/90) Kirzhner VM, Kordenko AN, Ushakov IB.

***Reactions of skin basophils of rats to exogenous hypoxia: A study of certain correlations.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 86 -88; 1989.

[1 references; none in English]

Histology, Skin Basophils

Rats

Hypoxia

**Abstract:** A study was performed on 47 white rats. Exogenous hypoxia was induced in an airtight chamber containing an atmosphere of 92% nitrogen and 8% oxygen. Immediately before exposure to the hypoxic medium a biopsy was taken of the left ear, and after 8 minutes exposure a similar biopsy was taken from the right ear. The biopsied tissue was fixed and embedded in paraffin. Samples 10  $\mu$ m thick were stained with toluidine blue at pH of 4.2. The number of  $\gamma$ -metachromatic (heparin-containing) tissue basophils were counted. Three structural features were selected as characteristic of the tissue basophils: the presence of basophils with a clear orthochromatic nucleus; cell shape (round, oval or spindle-shaped were considered normal, while those with outgrowths or surrounded by separate granules or clumps of granules, were considered abnormal); presence of areas of dense metachromasia or merely individual granules. On the basis of these characteristics, each of which was assigned a binary rating, the population of tissue basophils was divided into six morphological categories. Pairwise correlations between numbers of basophils belonging to various morphological categories were computed, along with the mean number of basophils in the various categories before and after hypoxia.

In animals not exposed to hypoxia, there are a number of rather large pairwise correlations (positive and negative) between different categories. In particular, there were negative correlations between numbers of basophils not showing signs of secreting heparin (with orthochromatic nuclei and normal cell shape) and secreting basophils (irregular shape). After hypoxia, there were no significant differences from baseline in mean quantities of different types of basophils. The tendency for secreting and nonsecreting forms to be correlated was retained. However, many correlations diminished in magnitude. There was a positive correlation between initial levels of a certain basophil type and extent of their decrease after hypoxia. This relationship increased intersubject similarity on these parameters. The authors argue that these results indicate that initial population of tissue basophils is a promising parameter for predicting individual reactions to environmental changes.

Table 1: Characteristics of various morphological types of tissue basophils in the skin of rats

Table 2: Quantities of tissue basophils in the skin of rats before and after exogenous hypoxia

Figure 1: Correlations between quantities of tissue basophils belonging to various morphological categories in the skin of rats before and after hypoxia

Figure 2: Correlations between initial quantities of tissue basophils in the skin of rats and their increase after hypoxia



### PAPERS:

P1169(26/90) \*Ponomarenko VA, Lapa VV, Nikitin IS.

***Psychophysical characteristics of sensorimotor performance of an operator after short-term exposure to simulated hypogravity.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 9-12; 1989.

[[11 references; none in English]

Human Performance, Sensorimotor Performance; Neurophysiology, Proprioception

Humans, Operators

Hypokinesia with Head-down Tilt, Immersion

**Abstract:** This work sought to identify the nature of the changes in operator performance occurring after short-term exposure to simulated weightlessness, and to determine how they affected performance on a task involving control of a moving object. As a simulation of weightlessness, subjects underwent 6 days of hypokinesia with head-down tilt ( $-10^\circ$ ) and 1 day of immersion. Testing was conducted in a set-up that simulated control of a moving object. Subjects were brought to the experimental set-up in head-down position and exposed to lower body positive pressure (up to 60 mm Hg). Three tasks varying in difficulty were used. The first involved control using instruments providing information on the position and movements of the object along a given trajectory. The second task required the operator to get the necessary information from general signals containing derived information about all parameters. This task required the operator to intervene to correct the course more rapidly, frequently, and accurately than the previous task. The third task involved on-line shifts in the requirements for accuracy as a function of various features of the trajectory. Performance accuracy was assessed using probability of correct performance with respect to the totality of task parameters. Perception of information (as displayed on instruments) was assessed on the basis of relative time spent monitoring the instruments, as measured by an eye movement recorder. Sensorimotor coordination was estimated from utilization of the horizontal and vertical control rudders, spectral characteristics of the controlling movements, and amplitude of the bioelectric activity of muscles of the right hand. Functional status of the kinesthetic sensory system was assessed on the basis of ability to reproduce and maintain a force of 10 kg for 10 seconds 10 times. Subjects were six pretrained operators, each of whom performed the control cycle eight times before and eight times after exposure to weightlessness.

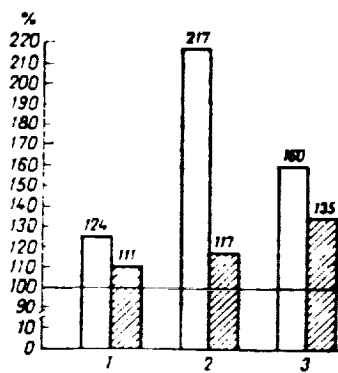
Exposure to simulated hypogravity did not affect control performance with respect to use of the horizontal control rudder. Decrements in the vertical component of performance were observed, but only for the two more demanding tasks. For the two more demanding tasks, use of vertical control rudders increased after treatment and bioelectric activity in the muscles of the controlling arm increased by an even greater percent over baseline. There was a pronounced shift in the spectral composition of the controlling movements toward higher frequency components. After hypogravity, amount of time spent monitoring instruments increased for all tasks.

The sum total of changes is described by the authors as suggesting loss of automaticity for the skills involved in object control. This they attribute to a change in the functioning of the proprioceptive system. This idea is confirmed by marked decrement of performance in maintaining a given muscle effort. The authors draw three practical conclusions from their study. First, when spacecraft must be piloted during readaptation to normal gravity, motor acts will be primarily regulated by the second (i.e., based on conscious symbolic information) signalling system, including mental image of spatial position of the spacecraft. Second, on-line monitoring of operator reliability and prediction of performance must include an evaluation of

## HUMAN PERFORMANCE

differential thresholds of proprioceptive sensitivity. Third, spacecraft crews should be trained to control the spacecraft under conditions of distortion of proprioceptive sensitivity.

Table: Comparative evaluation of level of control as a function of control task and exposure to simulated weightlessness



1.

Figure 1: Use of vertical control lever (white bars) and bioelectric activity of the flexor muscles of the right hand and fingers (hatched bars) after exposure to simulated hypogravity as a function of control task.

1,2,3 indicate tasks; horizontal line indicates baseline level

Figure 2: Smoothed standardized spectral evaluation of control movements in the vertical direction after exposure to simulated hypogravity

Figure 3: Functional status of the kinesthetic sensory system while reproducing and maintaining a stipulated muscle force after exposure to simulated hypogravity

Figure 4: Accuracy of reproduction of muscle force after exposure to simulated hypogravity

P1199(26/90) Bobko NA.

***Diurnal variations in the efficiency of operator mental performance in shift work.***

Fiziologicheskiy Zhurnal.

35(6): 83-87.

[20 references; 4 in English]

Author's Affiliation: Research Institute of Occupational Hygiene and Diseases, Ukrainian Ministry of Public Health

Human Performance, Shift Work; Cognitive Task

Humans, Operators

Biological Rhythms, Diurnal Variations

**Abstract:** The objective of this experiment was to identify changes in efficiency of mental task performance at various times of day under conditions of shift work. A total of 20 operators (machinists) working on three shifts (23:00-7:00, 7:00-15:00, and 15:00-23:00) served as subjects. The test involved mentally rearranging a set of 4 digits into ascending order. Parameters considered were time (measured in 1/50 second) and errors. Testing occurred at the end of the first hour of the shift and involved 30 trials. Each operator participated in 42 sessions (14 for each shift). Mean individual and group data were computed and tested for significance using Student's *t*.

No statistically significant diurnal variations were identified when data were averaged over the group. There was, however, a tendency for both errors and speed to decrease at 8:00 compared to 16:00, and 24:00. When individual data were examined it was found that 15% of the operators working on shifts displayed marked diurnal variations in efficiency of information processing as a function of which shift they were working, while 45% showed moderate variability. Speed of information processing was more prone to diurnal differences than error rate. The authors argue that the occurrence of statistically significant differences in mental performance as a function of different work shifts is a good diagnostic indicator for early identification of adverse effects.

Table: Diurnal variations in parameters of mental performance during shift work

## MONOGRAPH:

M155(26/90) Frolov AA.

Apparatura i Metody Issledovaniya Deyatel'nosti Operatory;

Аппаратура и Методы Исследования Деятельности Операторы

[*Apparatus and Methods for Investigating Operator Performance;*]

Moscow: Nauka; 1989.

[112 pages]

Affiliation: Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences

**Key Words:** Human Performance; Humans; Operators; Equipment and Instrumentation; Research Apparatus; Research Methods; Psychology; Neurophysiology

**Annotation:** The materials included in this collection are relevant to a broad range of issues having to do with the application of methods for analyzing experimental data in order to diagnose and predict the functioning of a human operator and assess the reliability and efficiency of his performance. A number of different devices for use in psychophysiological experimentation are proposed. This book is intended for specialists in psychological engineering and psychophysiology -- physiologists, psychologists, physicians, and engineers.

## Contents

Frolov MV, Andreyev IV, Milovanova GB, Sviridov YeP. The dynamics of superslow parameters of functional state in operators performing monotonous tasks (3)

Volkov VG, Larin IV. A simulator of pursuit tracking tasks using an ordinary television screen as a display (8)

Sel'tsovskiy PP, Pryakhin AB, Zhigareva RI. Use of psychophysiological examinations to predict certain aspects of the work-related reliability of vehicle drivers (12)

Andreyev IV, Yeryshalov VA, Tskhorebov AM. Apparatus designs for recording slow processes (18)

Sviridov YeP. Transitional processes in parameters of eyelid response in evaluating various functional states (22)

Potulova LA, Korinevskiy AV, Kosolapov AA, Kotrovskaya TI. Characteristics of the EEG of a human operator during detection of a meaningful light signal under conditions of heightened emotional tension (29)

Erashchenko NA, Vel'tishchev DYU. Rate of speech as a parameter of the leading type of depressive affect (41)

Grimak LP, Zvontskov VM. Modeling functional asymmetry of the brain using hypnotic suggestion (47)

Kolpakov SP, Leyserson YeYa. Evaluation of the effects of corrective measures on the interrelationship of far vision, accommodation amplitude and systemic blood flow during operator performance (51)

Taratynova GV, Podkletnova IM. Individual differences in the conceptual structure of visual images (56)

## **HUMAN PERFORMANCE**

Sorokina ND, Khachatur'yans ML, Zyablova NV. An entropy analysis of the variables of functional states (59)

Frolov MV. Gilbert filtration of biosignals of the harmonic type (69)

Ovchinnikov ND. An instrument for diagnosing operator state on the basis of brain lateralization parameters (73)

Avak'yan GN, Volkov VG, Mashkova VM. Psychophysiological methods of research in diagnosing and monitoring correction of disturbances in motor coordination (79)

Glazkova VA, Desova AA. A comparative assessment of the significance of information provided by the oscillating components of the slow frequency band in the rhythmic structure of sphygmo- and electrocardiograms (85)

Kovalev VP, Belichenko SV, Novototskiy-Vlasov VYu. The use of averaged evoked potentials in narrow reaction time intervals for analysis of operator performance (91)

Lisin VV, Luchshev VI, Nazarenko YuV. A psychophysiological investigation of parachute jumpers participating in a high altitude arctic expedition (97)

Zvonikov VM, Strel'chenko AN. Changes in certain psychological and motor function parameters of humans in hypnotic suggestion-induced simulation of hemispheric dominance (101)

Kolpakov SP. The interaction of accommodation amplitude, visual acuity, and systemic circulation in workers in jobs requiring precision, before and after a vision correction program (106)

P1173(26/90)\* Levinskikh MA, Sychev VN.

***Growth and development of one-celled algae as a component of an "algobacterial cenosis - fish" ecosystem under space flight conditions***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 32-35;1989.

[12 references; 1 in English]

Life Support System, CELSS; Algobacterial Cenosis-Fish Ecosystem

Microbiology, Algae, *Chlorella*; Fish

Space Flight; COSMOS-1187

**Abstract:** The primary subjects of this experiment were the green algae *Chlorella vulgaris* line LARG-1, a one-celled algae, with cells varying in size from 2 to 12  $\mu\text{m}$ , depending on age. The cells are round, the chloroplast calyciform, and the pyrenoid poorly defined. Reproduction occurs via autospores, 4 to 16 of which form in the mother cells. On board COSMOS-1887, *Chlorella* were placed in an algobacterial cenosis — fish ecosystem. The heterotrophic components of the system were 6 adult guppies with a total weight of 5 g. The experiment was performed in the "Aquarium" unit, which consists of a hermetically sealed acrylic plastic container with internal volume of 2.5 l. One wall was illuminated with a luminescent 8 volt lamp on a schedule of 16 hours of light alternating with 8 hours of darkness. Water temperature was maintained at  $24 \pm 2^\circ\text{C}$ , with the exception of the last few days, when, after landing, temperature dropped to  $10^\circ\text{C}$ . The total duration of the experiment was 18 days. The growth of the algae within the system was cumulative. The initial density of the algae suspension was selected so that the plateau period of growth would be reached during days 15-17. The algae were studied immediately after the flight material became available. The following properties were studied during initial processing: increase in number of cells and dry material; number of generations during the experiment; state of the population - assessed from number of dead cells, cells with lowered viability, cell size, percentage of dividing cells and number of autospores in mother cells; and age structure of the population.

Analysis showed active algal growth during the flight. The number of cells increased from 400,000 to 4.8 million per 1 ml, indicating that more than two generations had been produced. This growth was somewhat greater than in the laboratory control condition, but did not exceed maximum numbers obtained in pilot experiments and the synchronous control condition. Flight algae biomass increased according to a curve identical to those in the baseline and control conditions. Reproduction was normal. Number of cells with autospores was analogous to that of the control cultures. No disruption of spore formation was noted in the flight condition. The percentage of cells with reduced viability was somewhat elevated in the flight condition, but this difference is described as being within normal limits. No differences were found in percentage of dead cells. Average size of cells was lower in the flight group, in which very large cells were absent. Cells of all ages were represented in the flight group; however, the age composition was analogous only to the synchronous group and differed from other controls. There was a greater number of autospores and fewer cells with autospores in the flight and synchronous conditions. This is attributed to the decrease in temperature at the end of the experiment for these two conditions.

## LIFE SUPPORT SYSTEMS

Table 1: Characteristics of the growth of algae in the "Aquarium" experiment

Condition	Increase in # of cells, million/ml	Final density of dry substance, g/l	Productivity of algae in g dry substance	in % of flight value
Flight	4.8	0.12	0.26	100.0
Baseline	5.0	0.12	0.26	96.2
Laboratory	4.5	0.10	0.22	84.6
Synchronous	4.9	0.10	0.23	88.5

Table 2: State of the population and distribution of cells on the basis of physiological age in a *Chlorella* culture in the "Aquarium" experiment

Condition	Mean cell size, $\mu\text{m}$	Relative number with decreased viability, %	Relative number of cells with auto- spores	autospores	photosynth. active cells
Flight	3.4	7.0	3.0	45.0	52.0
Baseline	4.0	3.0	5.0	26.0	69.0
Laboratory	4.0	4.0	4.0	32.0	64.0
Synchronous	3.9	1.0	2.0	43.0	55.0

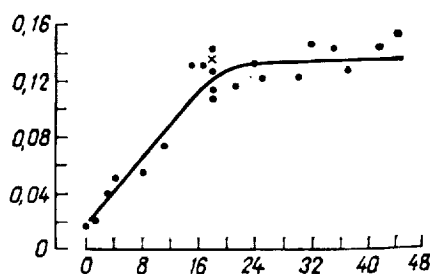


Figure: Dynamics of increase in *Chlorella* biomass being grown as a component of an "algobacterial cenosis-fish" ecosystem on the ground.

Abscissa: time (in days); ordinate: weight of dry substance of algae biomass (in g/l).  
X - final density of *Chlorella* population in flight condition

P1174(26/90)\* Sychev VN, Levinskikh MA, Livanskaya OG.

**Investigation of the growth and development of *Chlorella* exposed to space on COSMOS-1887.**

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 35-39; 1989.

[9 references; none in English]

Life Support System, CELSS  
Microbiology, Algae, *Chlorella*  
Space Flight, COSMOS-1887

Abstract: After *Chlorella* grown in space (as described in the previous abstract) were returned to the laboratory, the biological material was placed in a liquid balanced nutritive substrate intended for 19 g growth per 1 l suspension. The culture was illuminated for 24 hours a day at an intensity of 16-17 klx, at a temperature of 36°C, with concentration of 2-3% CO<sub>2</sub> in air blown through the suspension. The algae were cultivated on a cumulative schedule for 8 days. Each day a sample was removed and the parameters listed in the previous abstract studied.

No differences between flight and ground control cultures were observed in rate of growth. The usual S-shaped growth curve was followed. Lag period was equal to 1 day for both conditions. No differences were found in number of cells with reduced viability, or dead cells. No substantial differences were found in cell size or age distribution.

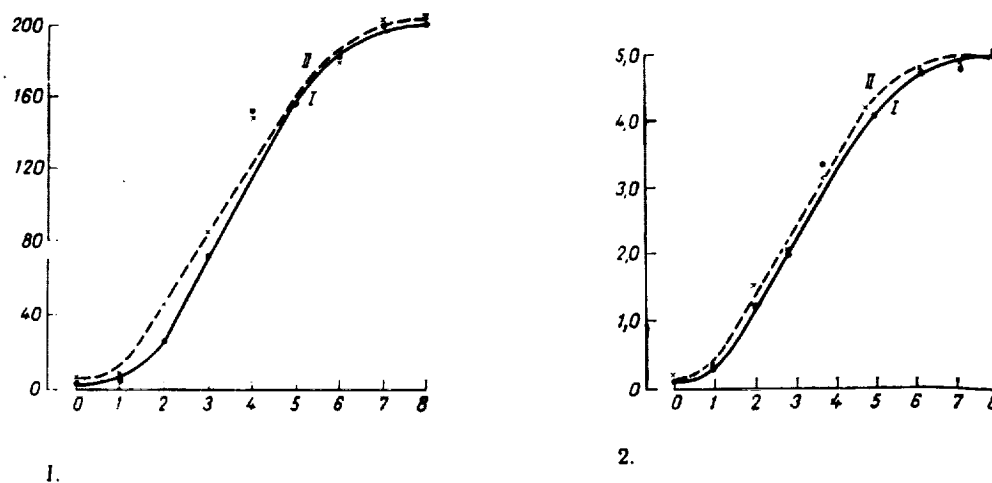


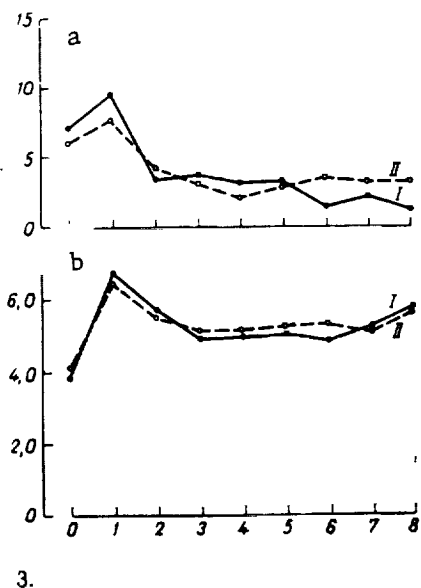
Figure 1: Dynamics of increase in number of algae cells grown under autotrophic conditions in a liquid medium with illumination of 16-17 klx

Abscissa - time (in days); ordinate; number of cells (in million per 1 ml). Here and Figures 2-4, I - flight condition; II — control

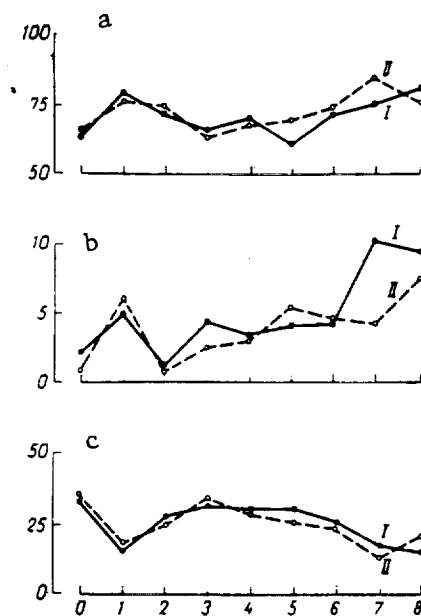
Figure 2: Dynamics of increase in dry biomass of algae cells grown under autotrophic conditions in a liquid medium with illumination of 16-17 klx

Abscissa - time (in days); ordinate - dry biomass of algae (in g/l)





3.



4.

Figure 3: Concentration of cells with depressed viability (a) and mean cell size (b) in "flight" and control cultures

Abscissa: time (in days), ordinate: a - % of total cells; b - cell size (in  $\mu\text{m}$ )

Figure 4: Concentration of individuals of various age groups: photosynthetically active cells (a), cells with autospores (b), autospores (c) in the "flight" and control cultures

Abscissa: time (in days); ordinate: percent of total number

P1175(26/90)\* Drugova NA, Chernova LS, Mashinskiy AL.

***The formation of a wheat microbial cenosis on a manned space flight.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 39-42; 1989.

[10 references; 1 in English]

Life Support Systems, CELSS

Botany, Wheat, Microbiology

Space Flight, Manned

**Abstract:** The goal of this experiment was to study a microbial cenosis forming on the leaves and roots of wheat plants undergoing vegetative growth on an inhabited spacecraft. Plants were grown in the "Svetoblok-M" chamber with a system of water and mineral supply in contact with the atmosphere of the inhabited cabin. An artificial ion-exchange substrate in tissue form was used. The substrate contained the following minerals in mole/kg: potassium - 0.30, calcium and magnesium - 1.46; iron (II) - 0.015; iron (III) - 0.01; nitrates - 0.03; phosphates - 0.09; sulfates - 0.375, and trace elements. Illumination was 9.5 - 30 W/m<sup>2</sup> and photosynthetically active radiation (depending on height of plant) was provided 24 hours a day. Sterile wheat seeds processed with tetramethyltiuramdisulfide were placed in the Svetoblok-M device on a dry substrate, which was moistened on board the spacecraft. The ground-based synchronous experiment utilized the same device, but without contact with an inhabited area. Initial materials obtained from rinsing of the internal surface of the growth device, and the leaves and roots of the plants were obtained on day 19 of growth, when the third leaf was beginning to appear. The latter two types of samples were obtained by vigorously shaking suspensions of the plant material in sterile tap water for 10 minutes. Koch's method was used to measure the total number of microorganisms. A meat-peptide agar served as the nutritive medium for the heterotrophs, while autoflora were identified on vegetable agar. Actinomycetes were identified on a starch-ammonia medium; fungi on an acidified Czapek medium, oligonitrophils on nonconcentrated Ashby? medium, and bacteria of the intestinal bacilli group on Endo medium. The method of limiting dilutions was used to perform a group analysis of the following functional groups of microorganisms: ammonia-fixing, denitrifying, celluloseolytic, and nitrifying bacteria. A quantitative analysis of the first three groups was performed after 5-7 days of incubation; nitrifying bacteria were measured after 3 weeks. A McReady table was used to count the number of microorganisms. Isolated pure cultures were identified based on morphological and physiological/biochemical features, using Bergey's Manual. Data were subjected to statistical processing.

Results showed that in an inhabited spacecraft module in flight, the number of bacteria on wheat leaves is higher than for a ground based uninhabited condition, with the increase in intestinal bacilli being most striking. All other microorganisms investigated were more numerous in the leaves of the plants grown in space. In the rhizosphere of plants no difference between experimental and control cultures was noted with regard to overall quantity of microflora. However, numbers of fungi and celluloseolytic bacteria were several orders of magnitude higher for the flight condition. Intestinal bacilli were found only in the experimental condition and actinomycetes only in the control. There were more fungi on the walls of the growth chamber in the experimental than in the control condition.

Cultivation of wheat under manned space flight conditions led not only to increased numbers of microflora, but also to increased variety. On the ground, the primary species to grow on the leaves were *Aspergillus* and *Penicillium*, while on the rhizosphere *Aspergillus*, *Penicillium*, *Cladosporium* and *Stemphylium* predominated. In space, the fungus *p. Cladosporium* was additionally present on the leaves, and *Mucor*, *Cephalosporium*, and *Verticillium* on the roots. Thus results show that the microbial cenoses developing on plants during the initial period of

## LIFE SUPPORT SYSTEMS

vegetative growth in a manned spacecraft are affected by the presence of man when there is contact through the substrate and atmosphere. Space cultures are marked by higher overall levels of bacteria and fungi on the leaves, and to a lesser extent on the roots, and by the presence of intestinal bacilli and increased numbers of cellulolytic bacteria.

Table 1: Microflora on the leaves of plants (number of organisms per 1 gram dry substance)

Microorganisms	Experimental	Control
Total level of bacteria on epigeal portion of plant	$(1.09 \pm 0.01) \cdot 10^8$	$(6.65 \pm 0.33) \cdot 10^7$
Plant autoflora	$(5.45 \pm 0.10) \cdot 10^7$	$(3.43 \pm 0.20) \cdot 10^4$
Fungi	$(1.05 \pm 0.02) \cdot 10^5$	$(1.02 \pm 0.02) \cdot 10^3$
Actinomycetes	not found	not found
Oligonitrophils	$(1.78 \pm 0.18) \cdot 10^6$	$(2.66 \pm 0.09) \cdot 10^4$
Denitrifying	$(2.27 \pm 0.05) \cdot 10^6$	not found
Ammonifiers	$(5.44 \pm 0.07) \cdot 10^9$ (sic)	$(1.22 \pm 0.04) \cdot 10^4$
Intestinal Bacilli Group	$(3.40 \pm 0.18) \cdot 10^2$	not found

Table 2: Microflora of the roots of wheat (number of organisms per 1 g dry substance)

Microorganisms	Experimental	Control
Total level of bacteria on plant rhizosphere	$(5.07 \pm 0.08) \cdot 10^9$	$(2.24 \pm 0.05) \cdot 10^9$
Plant autoflora	$(2.44 \pm 0.04) \cdot 10^9$	$(3.58 \pm 0.14) \cdot 10^8$
Fungi	$(6.73 \pm 0.04) \cdot 10^6$	$(5.89 \pm 0.18) \cdot 10^5$
Actinomycetes	not found	$(1.91 \pm 0.01) \cdot 10^4$
Oligonitrophils	$(3.98 \pm 0.02) \cdot 10^8$	$(7.17 \pm 0.10) \cdot 10^9$
Denitrifiers	$(4.40 \pm 0.07) \cdot 10^8$	$(7.18 \pm 0.09) \cdot 10^8$
Ammonifiers	$(2.20 \pm 0.05) \cdot 10^9$	$(6.22 \pm 0.08) \cdot 10^9$
Cellulosolytic	$(4.01 \pm 0.18) \cdot 10^5$	$(2.87 \pm 0.53) \cdot 10^3$
Nitrifiers	not found	not found
Intestinal Bacilli Group	$(8.14 \pm 0.29) \cdot 10^4$	not found

Table 3: Microflora from the inner surface of the Svetoblok-M unit (number cells per 100 cm<sup>2</sup>)

Microorganisms	Experimental	Control
Bacteria	$(9.64 \pm 0.11) \cdot 10^3$	$(3.56 \pm 0.42) \cdot 10^3$
Fungi	$(9.05 \pm 0.05) \cdot 10^3$	$(1.74 \pm 0.06) \cdot 10^3$
Intestinal Bacilli Group	not found	not found

P1185(26/90)\* Vasilenko II, Shevel' NM, Sinyak YuYe.

***Matter balance during the catalytic oxidation of water mixtures by hydrogen peroxide.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5) 75-78; 1989.

[11 references; 2 in English]

Life Support System, Water Regeneration, Catalytic Oxidation, Low Temperature  
Hydrogen Peroxide  
Matter Balance

**Abstract:** From the standpoint of energy economy of water regeneration for space flight, it is desirable to replace the traditional oxidative/catalytic process with one involving low temperature liquid-phase oxidation using hydrogen peroxide in the presence of oxides and other nonmetallic catalysts. This work investigated the relationships of gaseous products of catalytic reactions with varying concentrations of the oxidizer, and also the amount of water forming in these reactions. Removal of phenol from water was selected as the model. Materials used included 0.22 mm pieces of the mineral siderite, which contains 22.3%  $\text{Fe}^{2+}$  and water solutions of phenol and analytic grade hydrogen peroxide in a total of 10-20 ml liquid. Oxidation was performed at an initial temperature of 20-22°C and a magnetic stirrer was used. Kinetics of the catalytic processes were monitored on the basis of volume of  $\text{O}_2$  and  $\text{CO}_2$  produced. The amount of phenol conversion was computed using the equation:  $\alpha = (\text{CO}_2)/(\text{CO}_2)_T$ , where  $(\text{CO}_2)$  is the volume of carbon dioxide produced in phenol oxidation and adjusted to normal conditions and  $(\text{CO}_2)_T$  is the theoretical volume corresponding to the complete oxidation of phenol under the experimental conditions. The following systems were studied:  $\text{H}_2\text{O} - \text{H}_2\text{O}_2 - \text{C}_2\text{H}_5\text{OH} - \text{siderite}$ ;  $\text{H}_2\text{O} - \text{H}_2\text{O}_2 - \text{HCl} - \text{siderite}$ ;  $\text{H}_2\text{O} - \text{H}_2\text{O}_2 - \text{siderite}$ ;  $\text{H}_2\text{O} - \text{HCl} - \text{siderite}$

A general equation describing the kinetics of oxidation of phenol to yield  $\text{CO}_2$  was derived:  $V_{\text{CO}} = k_2[\text{C}_6\text{H}_5\text{OH}]^{0.55}[\text{H}_2\text{O}_2]^2[\text{Fe}^{2+}]^2$ , where  $\text{Fe}^{2+}$  is the iron in the catalyst. The oxygen produced by this process is described by the equation  $V_{\text{O}_2} = k_1[\text{H}_2\text{O}_2]^{1.46}$ . When concentration of hydrogen peroxide increased from 0.5 mole/l to 2.0 mole/l, the  $\text{CO}_2/\text{O}_2$  ratio increased from 12.8 to 87.2% with consumption of the oxidizer increasing from 39.2% to 46.6%. The conversion rate of 0.05 M  $\text{C}_6\text{H}_5\text{OH}$  to carbon dioxide after 35 minutes of oxidation in the presence of 0.5 g catalyst at 21°C was 99.8%. Chemical reactions between hydrogen in the impurities and oxygen in the hydrogen peroxide increase the amount of pure water produced by the process.

In space flight conditions, the daily production of liquid wastes is approximately 2 l per person. The mean concentration of organic contaminants in this waste is approximately equivalent to 0.05 M phenol. If these products are purified using the method employed here, an additional 204.4 kg water per year would be formed due to the chemical reaction.

The authors conclude that the proposed method of water reclamation would permit various organic substances unfit for direct use to be transformed into water and  $\text{CO}_2$  which can be reused. This would mean that it was no longer necessary to extract water from wastes that are difficult to process within space flight life support systems.

Table 1: Effect of concentration of hydrogen peroxide on the ratio between gaseous products and consumption of the oxidizer

Table 2: Conversion of phenol into carbon dioxide

## LIFE SUPPORT SYSTEMS

Figure 1: Kinetics of the production of oxygen in a  $\text{H}_2\text{O}$  -  $\text{HCl}$  - siderite. system

Figure 2: Effect of pH on production of carbon dioxide in a  $\text{H}_2\text{O}$  -  $\text{H}_2\text{O}_2$  -  $\text{HCl}$  - siderite system

### PAPERS:

P1178(26/90)\* Zaytsev LB, Larina ON, Popova IA.

***Serum proteins and products of nitrogen metabolism in humans undergoing long-term hypokinesia.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5) 50-53; 1989.

[7 references; 6 in English]

Metabolism, Nitrogen; Serum Proteins

Humans

Hypokinesia With Head-down Tilt, Long-Term; Countermeasures; Drugs; Physical Exercise

**Abstract:** It has been established that in hypodynamia, synthetic processes are inhibited and catabolic processes activated, leading to negative nitrogen balance and overall and organ weight loss. Results of previous work have shown that under these conditions certain prophylactic measures may foster some degree of normalization of metabolic processes. The increase in the length of time spent by cosmonauts on space stations poses new problems for researchers. The use of long-term hypokinesia, especially accompanied by head-down tilt, as a model of weightlessness enables a deeper understanding of observed changes in metabolic processes and also makes it possible to optimize the system of prophylactic countermeasures. The goals of the current investigation were to discover the effects of 370 days of hypokinesia with head-down tilt on blood proteins and concentrations of the final products of nitrogen metabolism in blood and urine and to evaluate the corrective effect of a set of prophylactic countermeasures.

Subjects were 9 healthy males, aged 27-42, undergoing a 370-day period of bedrest with head-down tilt (-5°). Of these subjects, 4 (group A), received a set of prophylactic measures, beginning on day 25 of treatment. These countermeasures included drugs intended to normalize calcium, mineral, and fluid-electrolyte metabolism, and pancreatic function, as well as a program of physical exercise. The remaining 5 subjects (group B) spent the first 120 days in strict bedrest (i.e., no prophylactic measures) after which they too utilized the countermeasures.

Measurements were made in serum of venous blood taken in the morning in a fasting subject at rest during the baseline period; on days 50, 110, 170, 230, 300, and 350 of bedrest; and on days 1 and 7 of the recovery period. Urine samples were collected over a period of 3 days. Blood serum parameters included total protein, protein fractions, and uric acid. Concentrations of creatinine and urea were measured in both serum and urine samples. The ratio of concentration of creatinine in daily urine to body weight was computed.

Protein fractions were separated using electrophoresis in an acetate cellulose film followed by staining and scanning on a digital integrating densitometer. The results of scanning, expressed in percentages of total protein concentrations, were translated into concentration units. The remaining parameters were measured using an automated analyzer. Statistical processing of the data was performed using the parametric Student's *t* criterion.

On day 50 and during the second half of the treatment period, subjects in both groups displayed a reliable increase in the concentration of total protein compared to the baseline period. This may reflect change in the rates of synthesis and decay of individual proteins, as well as redistribution of fluids in the vasculature, lymphatic system, and intracellular and interstitial fluids. The concentration of albumin reliably increased in subjects in group A in the final phase of bedrest; in subjects in group B this parameter did not change significantly compared to baseline.

## METABOLISM

Changes over time in concentrations of total globulins were similar to changes in concentrations of total protein. The concentration of  $\alpha_1$ -globulins decreased in group A and increased in group B. The decrease in concentrations of  $\alpha_2$ -globulins observed in both groups is a symptom of depression of biosynthetic activity of the liver, accompanied by low level of energy-forming processes in hypokinesia. In group B, there was a partial recovery of concentration of  $\alpha_2$ -globulins during the final phase of bedrest.

Concentration of  $\beta$ -globulins increased in both groups during bedrest, as is consistent with previous results. This fact may be associated with the finding in the literature that low density lipoproteins (atherogenic lipoproteins), which are a component of  $\beta$ -globulins, increase during hypokinesia. This result, in conjunction with the decrease in levels of  $\alpha_1$ -globulins, which contain high density lipoproteins (antiatherogenic lipoproteins), in group A, attests to the adverse effects of hypokinesia on lipid metabolism.

During the initial period of hypokinesia with head-down tilt, concentration of  $\gamma$ -globulins were elevated compared to baseline. Subsequently this parameter decreased reliably compared to the initial period of bedrest in both groups A and B. In the latter, this decrease was noted starting on day 170 and in the former on day 290 with the decrease during recovery more pronounced in group B.

During the recovery period, concentration of total protein and albumin increased, while concentration of  $\alpha$ -globulins decreased. Changes in  $\beta$ -globulins were in opposite directions for the two groups.

In this experiment, as in those performed earlier utilizing shorter periods of hypokinesia with head-down tilt, there was an increase in concentration of creatinine in blood accompanied by increased excretion, as duration of hypokinesia increased. However, during the first half of the experiment (up to 170 days), the prophylactic countermeasures utilized in group A supported the maintenance of a normal level of creatinine in blood and urine. During the second half, the prophylactic exercise program performed by both groups did not prevent the adverse effects of hypokinesia on nitrogen metabolism: the creatinine coefficient in all subjects exceeded normal values, indicating the predominance of catabolic reactions in the metabolic processes.

Concentration of urea in blood and the amount of urea excreted are determined to a great extent by the concentration and assimilability of protein in the diet, the level of physical activity, and also the functional status of the kidneys. These parameters were maintained during the experiment within the universally accepted norms, with the exception of a decrease in excretion of urea below the norm in group A on day 50. At certain points, the level of blood urea in group A was higher than baseline, while in group B excretion of urea was elevated on day 230. These fluctuations are attributed to changes in type of exercise performed.

Concentration of uric acid in blood during hypokinesia in both groups was within the bounds of the physiological norms, and the changes were in the same direction in both groups; however, they were more pronounced in group B. A decrease in the concentration of lactic acid in blood on day 50 of bedrest, and also in the second half of the experiment suggests some decrease in the rate of nucleoprotein and nucleic acid metabolism.

Taken in their entirety, the data obtained support a conclusion that the values of the parameters studied did not diverge significantly from the norm, with the exception of renal excretion of creatinine. Corrective effects of the prophylactic countermeasures was observed during the first half of treatment, up to day 170. During the second half of hypokinesia, there was an increase in the creatinine coefficient as a consequence of the predominance of catabolic processes over anabolic, and also a decrease in the concentration of lactic acid in blood, which

## METABOLISM

evidently reflects suppression of nucleic acid metabolism accompanying disruption of lipid metabolism, resulting in increased levels of low density lipids. Fluctuations in the concentrations of urea and total protein may be associated with the type of exercises included in the conditioning program, as well as vitamin and protein supplements.

The post-treatment recovery period was characterized by subbaseline levels of urea and uric acid in blood and decreased excretion of urea and creatinine, suggesting that nitrogen metabolism had not yet normalized.

Table 1: Concentration of total protein and protein fractions (in g/l) in blood serum of subjects

Parameter	Group	Baseline		Hypokinesia (days)					Recovery + 7
			50	110	170	230	300	350	
Total protein	A	70.6	73.9*	72.2	74.5	75.4	75.1*	74.6	71.8
	B	70.7	73.4*	72.4	69.2	71.9	71.9	74.0*	69.5*
Albumins	A	42.5	42.6	43.8	43.6	44.6	45.7	45.8	42.7
	B	44.5	42.4	45.4*	43.7	45.5	45.0	46.1	43.4
Globulins: total	A	28.2	31.3*	28.4	31.0*+	30.9*	29.4	28.8	29.2
	B	26.2	31.0*	27.0	25.5	26.4	26.9	27.8	26.2
$\alpha_1$	A	1.72	2.04	1.70	1.92	1.80	1.75	1.40	1.95
	B	1.64	1.98	1.82	1.82	1.86	1.92*	1.96	2.14*
$\alpha_2$	A	5.98	5.74	5.20*	5.75	5.12	5.08	4.65	5.48
	B	5.72	6.02*	5.58	4.90	4.76*	5.20	5.18	5.56
$\beta$	A	7.48	9.02	7.90	8.52	9.18**	9.20**	9.38**	9.40*
	B	8.08	9.62*	8.28	8.26	9.08**	9.09*	9.74*	8.98*
$\gamma$	A	13.0	14.5	13.6	14.4	14.8+	13.2+	13.1	12.5+
	B	10.7	13.3*	11.3	10.5	10.7	10.4	10.9	9.3

Here and in Tables 2 and 3, \* - differs from baseline with  $p < 0.05$ ; \*\* differs from baseline with  $p < 0.01$ ; + two groups differ with  $p < 0.05$

[Note: Differences noted as significant do not always seem consistent with difference magnitudes and standard deviations (given in original).

Table 2: Concentration of urea in blood serum (in mmole/l) and urine (in mmole/day) in subjects

Condition	Time	Blood serum		Urine	
		Group A	Group B	Group A	Group B
Baseline	- -	6.15	7.45	514.8	302.0
Bedrest	50	5.53	6.17	307.0**	351.2
	110	7.05	6.33	466.2*	354.6
	170	6.26	6.59	414.0	458.6
	230	7.18	6.55	448.5*	427.6
	300	5.86	5.63	443.6*	378.2
	350	6.85	6.77	483.5	339.0
Recovery	1	5.03	4.74*	352.5	242.4*
	7	4.94	4.36**	—	—



## METABOLISM

Table 3: Concentration of uric acid (in  $\mu\text{mole/l}$ ) in blood serum

Condition	Time, days	Group A	Group B
Baseline	---	353.6	361.4
Bedrest	50	341.6	311.8
	110	356.6	368.4
	170	334.0	384.2
	230	299.0	307.0
	300	308.5	314.0
	350	350.7	353.8
Recovery	1	276.7	313.0
	7	285.3	266.8**

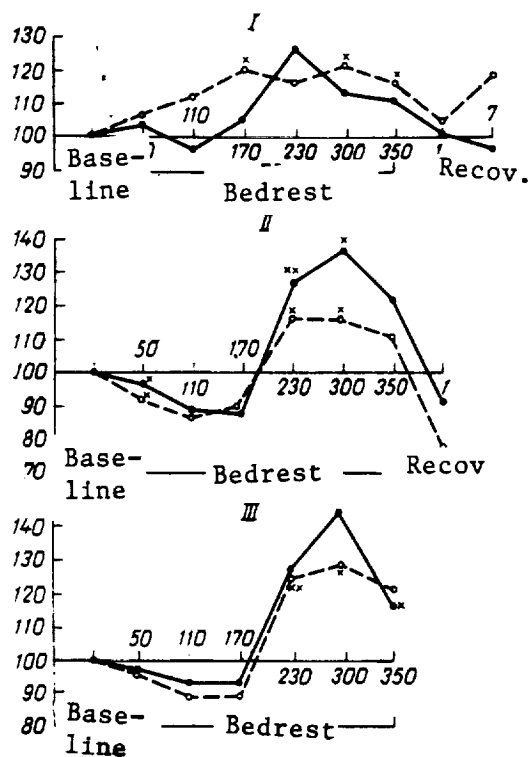


Figure: Changes in concentration of creatinine in blood serum (I), creatinine in urine (II) and value of creatinine coefficient (III)

Abscissa: duration of period (in days); ordinate: parameters value (in %). Solid line -- Group A; dashed line -- Group B. BP -- baseline period.. \* -  $p < 0.05$ ; \*\* -  $p < 0.001$  compared to baseline

P1195(26/90) Kuznetsov VI, Sarayev YuV, Chirkin AA.

**Activation of glycolysis, decreased glycogen reserves and lack of glucocorticoid control of enzymes of carbohydrate metabolism in the liver of rats undergoing long-term hypokinetic stress.**

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1989(4):56-59.

[13 references; 3 in English]

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Metabolism, Carbohydrate; Glycolysis; Enzymology

Rats, Males

Hypokinesia, Long-Term; Immobilization Stress

**Abstract:** The objective of this work was to evaluate glycogen reserve, ratio of glycolysis to glyconeogenesis in the liver, and also the activity of key glucocorticoid-dependent enzymes under long-term exposure to hypokinetic stress. Experiments were performed on 76 outbred male rats housed in individual cages with the head restrained, severely limiting motor activity. The rats received water and balanced feed *ad lib*. On days 5, 15, 30, 45, and 60 of stress the animals were sacrificed by decapitation. Concentration of 11-oxycorticoids (11-OC) in blood plasma were measured spectrophotofluorometrically; concentration of glucose was determined using the glucose oxidase method. The quantity of glycogen in the liver was measured. Liver homogenates were prepared at 2-4°C on an isolation medium. Enzyme activity was measured in a microsomal-cytoplasmic fraction obtained through centrifugation of homogenates in a refrigerated centrifuge at 18,000 g. Activity of the key glycolysis enzymes — phosphofructokinase (PFK) and gluconeogenesafructoso-1,2-biphosphatase (FBP) was determined. Concentration of protein in the microsomal-cytoplasmic fraction was also measured. Specific activity of the enzymes was calculated per 100 mg protein.

Concentration of 11-OC in plasma increased by 84% on day 5 of treatment, decreased almost to baseline on days 15-30, and increased again by 51-85% on days 45-60. Glycogen in the liver on day 15 did not alter significantly, but began to decrease subsequently and by days 45-60 had diminished by a factor of 2.4(sic.)-2. Level of glucose exceeded baseline only on days 5 and 45.

PFK activity per 100 mg protein decreased on day 5 by a factor of 2.4, normalized on day 15, dropped again on day 30, and then increased continually so that by the end of month 2, it exceeded the control level by a factor of 2. FBP activity per 100 mg protein was elevated only on day 5 of treatment. The increase in plasma 11-OC on day 5 of treatment attests to an acute stress reaction; typical of this response are opposite changes in activity of key glycolytic enzymes (decreased FPK activity) and in enzymes responsible for glyconeogenesis (increased FBP activity). Thus, on day 5 of stress, key enzymes of glycolysis and glyconeogenesis were under strict hormonal control, with clear predominance of glyconeogenesis over glycolysis, resulting in increased glucose in blood. A similar situation occurred on days 45-60 of treatment, suggesting that the stress response system had not yet become exhausted. The situation on day 45 (unaltered FBP activity, decreased FPK activating decreased glycogen in the liver)suggests disruption of hormonal control of FBP. On day 60 activity of FPK unexpectedly increased by a factor of 2, suggesting that glycolysis predominated over glyconeogenesis. Activation of FPK despite elevated blood 11-OC attests to the inability of 11-C to inhibit activity of this enzyme, i.e. loss of hormonal control. Thus, during long-term continuous exposure to a stress situation, sensitivity of enzymes of carbohydrate metabolism to hormonal control by 11-OC decreased. This also explains the desensitization occurring in the liver. The decrease in the glycogen depot in the liver may be significant in a shift from chronic stress to physical activity when glucose must be mobilized for muscular activity.

**Table: Concentration of 11-OC and glucose in blood plasma and parameters of carbohydrate metabolism in the liver of rats exposed to hypokinetic stress**

## MONOGRAPH:

M152 (26/90)Parfenov GP.

Невесомость и Элементарные Биологические Процессы; *Nevesomost' i Elementarnyye Biologicheskiye Biologicheskiye Protsessy, [Weightlessness and Elementary Biological Processes];*

Volume 57 In series: Problemy Kosmicheskoy Biologii,

Leningrad: Nauka; 1988.

[272 pages; 46 Tables; 26 Figures; 631 references]

**KEY WORDS** Microbiology, Precellular Organisms, One-Celled Organisms, Botany, Plant and Animal Cells, Cytology, Histology, Tissue Cultures; Space Flight, Radiobiology, Ionizing Radiation

**Annotation:** This monograph reviews the results of experiments performed on precellular and one-celled organisms, plant and animal cell and tissue cultures, on fungi, actinomycetes, higher plants, and insects. It covers virtually all experiments performed in space, including those that investigated the combined effects of weightlessness and ionizing radiation, and also the most interesting experiments using clinostats and centrifuges.

## CONTENTS

Foreword (5)

Introduction (8)

Chapter 1: Microorganisms (12)

1.1 Bacteriophages and viruses (14)

1.2 Procaryotes (17)

1.2.1 Bacterial spores (17)

1.2.2 Bacterial cells (23)

1.2.3 Lysogenic bacteria (28)

1.2.4 Blue-green algae (40)

1.3 Eucaryotes (41)

1.3.1 *Chlorella* (41)

1.3.2 *Chlamydomonas* (50)

1.3.3 Yeast (50)

1.3.4 *Penicillium* (55)

1.3.5 Neurospores (55)

1.3.6 Protozoa (57)

1.4 Conclusion (60)

Chapter 2: Cultures of animals cells and tissues (66)

2.1 Experiments on balloons (66)

2.2 Experiments without culture thermostating (67)

2.3 Experiments with culture thermostating (68)

2.4 The combined effects of weightlessness and ionizing radiation on cell cultures (72)

2.5 Chromosome rearrangement in *in vivo* blood cells (74)

2.6 Cytogenic changes in cells of the hemopoietic organs of mammals (76)

2.7 Conclusion (76)

## Chapter 3: Fungi and actinomycetes (78)

- 3.1 Actinomycetes (81)
- 3.2 The "Zonoforming? fungi-Biorhythm" experiment (82)
- 3.3 The MEED (Microbial Ecology Evaluation Device) experiment (83)
- 3.4 Experiments on COSMOS-690 (84)
- 3.5 Phycomycetes (86)
- 3.6 Conclusions (93)

## Chapter 4: Plants (98)

- 4.1 Experiments on dry seeds (98)
  - 4.1.1 Experiments on balloons and ballistic rockets (98)
  - 4.1.2 Experiments on descent modules (99)
  - 4.1.3 The Biostack and Bioblock experiments (106)
  - 4.1.4 The combined effects of space flight factors and ionizing radiation (108)
- 4.2 Experiments on plant bulbs (116)
- 4.3 Experiments on plant sprouts (118)
- 4.4 Plant orientation (130)
- 4.5 Experiments on *tradescantia* (138)
- 4.6 Cultivation of plants under conditions of weightlessness (145)
- 4.7 Epinasty of plant organs (154)
- 4.8 Nutational movements of plants (157)
- 4.9 Plant cell cultures (158)
- 4.10 Plant tumors (165)
- 4.11 Conclusion (165)

## Chapter 5: Insects (170)

- 5.1 *Drosophila*
  - 5.1.1 Experiments on balloons and ballistic rockets (172)
  - 5.1.2 Experiments on spacecraft (175)
    - 5.1.2.1 Recessive deaths and observable mutations (175)
    - 5.1.2.2 Dominant lethal mutations (178)
    - 5.1.2.3 Primary nondisjunction of sex chromosomes in females (179)
    - 5.1.2.4 Induced crossing over in males (181)
  - 5.1.3 Experiments on Soviet biosatellites (183)
  - 5.1.4 Experiments on Biosatellite-2 (189)
  - 5.1.5 Morphological and anatomical studies (191)
  - 5.1.6 Research on the ecological significance of weightlessness (195)
  - 5.1.7 Laboratory experiments with altered gravity (199)
- 5.2 Flour beetle (202)
- 5.3 *Habrobracons* (210)
- 5.4 Conclusion (212)

## Chapter 6: Evolutionary significance of gravity (221)

- 6.1 The force of gravity as the creator of the abiogenic environment (222)
- 6.2. Comparative physiological importance of electromagnetic and gravitational forces (225)
- 6.3 Thermodynamic prerequisites for the existence of living organisms (225)
- 6.4 Chemical and biological evolution (232)
- 6.5 The force of gravity as a factor in natural selection (230)
- 6.6 Physiological significance of the force of gravity

## Chapter 7: General conclusion (237)

## References (240)

## Chapter 7: General Conclusion

The material presented supports the following general conclusions regarding the effects of weightlessness and/or the force of gravity on biological subjects and processes.

1. Experiments with one-celled organisms have shown that weightlessness does not affect their survival rate, rate of reproduction, likelihood or number of mutations, morphology or biochemical parameters. Individual one-celled organisms showed no signs of any gravity-dependent processes.
2. The gravity independence of elementary biological processes in individual cells, the dimensions of cells and their general morphology, are determined by the second law of thermodynamics and for this reason are invariant with respect to space and time.
3. Research on cell and tissue cultures of humans and other mammals showed that responses to changes in the force of gravity are the prerogatives of systems no smaller than the organs, and most often of the organism as a whole. Altered gravitational force has identical effects on any cells that are similar in shape and size.
4. Cultivation of fungi in the absence of gravity does not alter their cellular structures, capacity for various forms of reproduction, adherence to the substrate, or dominance of apical growth. Fungi cultivated in weightlessness show disorganization of the direction of growth, which becomes random. Thus, in weightlessness, fungi retain all their properties, with the exception of gravitational coordination.
5. In weightlessness, all stages of development of higher plants: sprouting of seeds and formation of primary organs, differentiation and formation of somatic tissues, establishment of generative cells and maturation of generative organs, fertilization, and embryogenesis, maturation of seeds can progress normally. If we limit ourselves to processes describable in terms of molecular biology, biochemistry, and genetics, then we must conclude that elementary biological processes in plants proceed unaltered in weightlessness.
6. Under conditions of weightlessness plants undergo changes in all types of organ movement: geotropic orientation, circumnutation, and movements determining epinasty. One would expect changes in the final shape of plants cultivated in weightlessness, since plant movements are irreversible. However, the general shape of the plant remains the same.
7. Weightlessness has a dual effect on plants: since it does not affect the elementary processes and is only a secondary transformer of shape, weightlessness does not have a significant direct effect on their vital processes. But since the force of gravity is one of the major factors forming the substrate and atmosphere, its importance to the life of plants is obvious. The influence of weightlessness on plants may in this sense be studied and understood within the framework of ecological physiology when experiments are performed in which the major independent variable is altered force of gravity.
8. The results of research on the *Drosophila*, confirmed by data obtained on the flour beetle and *Habrobracon*, have shown that under conditions of weightlessness there are no increases in any of the major forms of spontaneous mutations that can be identified through hybridologic and cytogenetic tests.
9. When *Drosophila*, flour beetles, and *Habrobracon* are exposed to the combined effects of weightlessness and  $\gamma$ -irradiation in a wide range of doses, there are no synergistic or antagonistic effects in the substantial majority of genetic, physiological, and behavioral tests.

10. The alternation of generations in *Drosophila* and flour beetles proceeds unimpeded by weightlessness, and duration of various stages of development are not appreciably altered. When the processes of biological development are rigidly constrained, as in insects, the effects of weightlessness are insufficient to disrupt them even slightly.
11. Basically, the magnitude and direction of the force of gravity can only be perceived through various sensory systems. *Drosophila* have no sensory system that responds to the magnitude of gravity. Alteration in the force of gravity in the range of 0 g to several g units are not perceived by individuals of this species.
12. The genetic, morphological, and physiological status of organisms existing today is, to a significant degree, a consequence of the effects of gravity, which act in three different but interrelated ways: as the force responsible for the nature of the abiotic living environments; as an important factor in natural selection; and as a factor in ecological physiology creating mechanical stress. The influence of gravity in these roles is realized through various mechanisms and has various time frames.
13. Certain morphological properties, particularly the dorsoventral polarity of the body, are adaptations which have only phylogenetic significance. They arose as adaptations to an environment, shaped by the force of gravity, a vector structure. We call this effect a first order effect.
14. The significance of gravity as one of the abiotic components of natural selection should be considered a second order factor acting on biological organisms. The importance of gravity in this role increases as the size of the organism increases. In this role, gravity determines the upper limit of size, at least for land animals.
15. Study of the third order effect of gravity is also appropriate in physiology. For space biology and medicine, physiological research in this area is of critical significance, since data on gravitational physiology determines many aspects of the day to day activities on manned space flights. The effect of altered gravity in physiological experiments involves sensing (reception) of gravity and, in humans, consciousness of gravity as well. Working hypotheses relating to gravitational physiology are amenable to experimental verification.

## MUSCULOSKELETAL SYSTEM

### PAPERS:

P1176(26/90)\* Oganov VS, Rakhmanov AS, Ternovoy SK, Novikov VYe, Dubonos SL.  
***Mineral density of skeletal bones in humans exposed to simulated microgravity.***  
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.  
23(5): 43-46: 1989.  
[21 references; 11 in English]

Musculoskeletal System, Skeletal Bones, Mineral Density  
Humans  
Hypokinesia With Head-Down Tilt; Countermeasures; Physical Exercise

**Abstract:** The work reported on here was part of a study of the effects of a 370-day period of hypokinesia with head-down tilt and had as its goal determination of the sources of the greatest calcium loss in the skeleton, the temporal pattern of these losses, and their amenability to corrective countermeasures. Nine people, aged 27-41, participated in the study. All subjects were subjected to hypokinesia with head-down tilt (-5°) for a period of 370 days. Subgroup A (n=4) engaged in a physical exercise program throughout the period. Subgroup B began exercise on day 120 of treatment. Mineral density of spongy bone in the lumbar vertebrae LI-LIII was measured by quantitative computer tomography. Measurements were made several days before treatment started and on days 2-4 after its completion. The method of dual photon absorptiometry was also used to measure this parameter. Linear mineral density of lumbar vertebrae LII-LIV, including the vertebral body and the spinous and transverse processes, was measured with a densitometer. The same method was used to analyze mineral density of various areas of the femur, including the neck and the diaphysis. These measurements were made before treatment and every 2 months during it. The value of linear mineral density of the diaphysis of the bones of the calf and forearm (tibia, ulna, and radius) were measured using monophoton absorptiometry. Results were statistically processed and tested.

Computer tomography results revealed diminished mineral density in the spongy bone of lumbar vertebrae after hypokinesia in one subject in group A (by 12%) and one in group B (30%). In both cases, decreases were most marked at level LIII, leading to decrease in the normal positive density gradient in the LI-LIII direction. In four subjects, this same parameter increased by 11-27%, to a greater extent in group B. Mean group parameters remained virtually unchanged. Data from dual photon absorptiometry agreed with results of computer tomography. After treatment, mineral density of the vertebra (spongy and compact structures) did not decrease in the majority of subjects. The exception to this was the single subject in group B who showed a decrease in computer tomographic parameters. In this subject, physical exercise, starting on day 120, helped to normalize this parameter, but normalization was not complete. In some subjects absorptiometry revealed slight increases in vertebrae mineral density.

The most striking result revealed by densitometry took place in the neck of the femur, mineral density of which decreased in all subjects. Most extreme results occurred in one Group A subject (by 21%) and two group B subjects (by 18%). Group data showed different temporal patterns. On day 120 of treatment, group A subjects showed no decrease, and group B subjects a 67% decrease. Subsequent to this the parameter decreased in both groups. During days 240-370, the parameter normalized in group A and stabilized at 90% baseline in group B. Mineral density of the diaphysis of the femur decreased only in one group A subject, toward the middle of treatment, and in two group B subjects during the second half of treatment. Group means did not alter significantly.

Densitometry of the tibia bone revealed a decrease in mineral density up to 10% in three subjects in group A between days 120-300 of treatment; this parameter increased in one group A subject. In group B virtually all subjects showed some decrease in this parameter at some



## MUSCULOSKELETAL SYSTEM

point during the study. Differences in group means indicate an earlier decrease in this parameter in group B. Measurement of mineral density of the forearm bones, performed only pre- and post-treatment, revealed no significant differences in any subject; group means increased somewhat.

The authors conclude that concerns about decreased bone strength should be focussed first on the epiphysal zones, where decrease in mineral density were more regular and rapid. However, the absolute amount of calcium loss in these zones was relatively small. Decrease in mineral density of the diaphysis was not always noted and typically did not exceed 1% per month. At the same time, when the ratio of mineral mass of compact and spongy bone is considered, it should be noted that absolute calcium loss from compact structures may be considerable under conditions of long-term exposure to weightlessness and hypokinesia.

The marked decrease in mineral density of the neck of the femur is considered to be the first reliable indication of the possible source of calcium loss in response to weightlessness and hypokinesia. Since all subjects used prophylactic measures, this study does not reveal whether decreased mineral density in hypokinesia is self limiting. The importance of beginning exercise early in the hypokinesia process was demonstrated. Subjects were found to show a significant amount of individual differences in decreases in mineral density, the temporal pattern of such decreases, and response to prophylactic exercise.

Table: Results of bone tissue densitometry in an experiment involving 370 days of hypokinesia with head-down tilt

Parameter	Grp	Time, days						
		0	60	120	180	240	300	370
Mineral density of spongy bone, g/cm <sup>3</sup>								
Vertebrae	A	155	- -	- -	- -	- -	- -	157
	B	142	- -	- -	- -	- -	- -	150
Mineral density, g/cm <sup>2</sup> :								
Vertebrae	A	1.04	1.02	1.04	1.05	1.05	1.08	1.08
	B	1.00	0.99	1.03	1.03	1.02	1.00	1.00
Neck of femur	A	0.90	0.87	0.91	0.85	0.82	0.83	0.89
	B	0.84	0.81	0.79	0.77	0.77	0.75	0.75
Femur diaphysis	A	1.75	- - -	- - -	1.74	1.78	1.76	1.78
	B	1.69	1.69	1.68	1.68	1.66	1.71	1.70
Tibia	A	1.77	- - -	1.73	- - -	1.75	1.82	1.86
	B	1.61	1.58	1.57	- - -	1.56	1.64	1.61
Forearm bones	A	0.76	- -	- -	- -	- -	- -	0.80
	B	0.78	- -	- -	- -	- -	- -	0.81

P1196(26/9) Volozhin AI, Amelkina.GV.

***Changes in the periodontium in long-term hypodynamia and the use of diphosphonates and silatran to prevent these changes.***

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[12 references; 1 in English].

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Musculoskeletal System, Periodontium

Rats, Males

Tail Suspension; Prophylactic Countermeasures; Silicon; Diphosphonates

**Abstract:** Three experiments were run on male Wistar rats. In experiment 1 the animals were divided into two groups, a control (group 1), and an experimental group subjected to "tail suspension" to eliminate gravitational loading on the hind legs. In experiment 2 the experimental group underwent 40 days of suspension during which they were injected with a solution of 10 mg of a silatran (organic silicon compound) once every 3 days. Silicon compounds are considered to have a beneficial effect on bone tissue formation and mineralization. In the third experiment both groups were suspended and received diphosphonate preparations. Group 1 received 3-dimethylamino 1-hydroxypropylethene (DAP) in a dosage of 0.81 mg/kg and group 2 received 1-hydroxyethylidene diphosphonic acid (EDP) in a dose of 20 mg/kg. After termination of the experiment, all the animals were sacrificed and their lower and upper jaws isolated. The level of atrophy and microhardness of the bone tissue were assessed and a pathomorphological analysis conducted. Atrophy of the alveolar process in the upper and lower right and left jaws was rated on a 4-point scale for each of the 3 teeth and the mean score computed. Microhardness of bone tissue was measured in defatted and dried polished sagittal sections of the upper jaws that had been embedded in plastic. Pathomorphological studies utilized bone that had been cleaned of soft tissue, fixed, decalcified, made into histological sections, and stained.

Control rats displayed some spontaneous atrophy of the alveolar process, which varied in severity for different teeth. Tail suspension significantly altered the pattern of atrophy. There were fewer subjects with degree II atrophy and more with degree IV in teeth 2 and 3. The 40-day tail suspension period was associated with the formation of periodontal pockets, thickening of the covering epithelium, and vegetation in the underlying connective tissue. Phenomena noted in the connective tissue of the gum included thickening of fibers, hyalinosis, and papillomatosis of the covering epithelium. The gingival cleft was generally enlarged. The interdental and inter-root (interalveolar?) septa were smoothed with many adhesion lines. The surface of the bony alveoli was uneven, due to resorption lacunae. Haversian canals were enlarged in bone tissue. The experimental animals had fewer osteoblasts. Histological examination suggested that bone formation was depressed rather than resorption enhanced. Microhardness was depressed in experimental animals in all three teeth studied. Use of silatran had a significant corrective effect on parameters of atrophy in the alveolar process. In animals given this preparation, there were no signs of resorption of interalveolar and interdental septa, and less enlargement of the gingival cleft. In the third experiment, use of the diphosphonate DAP was associated with decreased atrophy, while microhardness parameters were increased especially where they had decreased most in response to hypodynamia, in the upper alveolar process. Use of EDP had a less significant effect on atrophy and did not improve microhardness in experimental animals.

Table: Microhardness in various areas of the upper jaw in control and experimental rats

Figure 1: The effect of hypodynamia on atrophy of the alveolar process in rats

Figure 2: Effects of diphosphonate on atrophy of the alveolar process in rats undergoing hypodynamia

# MUSCULOSKELETAL SYSTEM

## MONOGRAPH:

M157(26/90) Stupakov GP, Volozhin AI.  
Kostnaya Sistema i Nevesomost'; Костная Система и Невесомость  
[*The Skeletal System and Weightlessness*].  
Volume 63 In series: Problemy Kosmicheskoy Biologii,  
Leningrad: Nauka; 1989.  
[184 pages; 27 Tables; 44 Figures; 317 References; 201 in English]

Musculoskeletal System, Skeletal System  
Humans, Cosmonauts; Rats, Tortoises  
Space Flight, Long-Term

Annotation: This book cites data concerning changes in bones of cosmonauts on long-term space flights. Using data from experiments performed on rats and tortoises, the authors describe changes in bones in various portions of the skeleton, consider level of recovery, and cite data concerning the effects of gravitational unloading of bone on its physical and mechanical properties. The book is intended for specialists in the area of space biology, physiologists, and pathophysiologists.

## CONTENTS

Introduction (5)

Chapter 1 Structural and functional characteristics of bone tissue (7)

- 1.1 Structural levels of bone tissue (7)
- 1.2 Organic components and mineral phase of bone tissue (9)
- 1.3 Cellular composition of bone tissue and modeling mechanisms (16)
- 1.4 Remote regulators of bone tissue metabolism (26)
- Conclusion (36)

Chapter 2 Research methodology (36)

- 2.1 Research on restructuring and state of the mineral components of bone tissue (36)
- 2.2 Methods for determining the element composition of bone (38)
- 2.3 Research on the mechanical properties of bone (41)

Chapter 3 The skeletal system of experimental animals exposed to weightlessness (47)

- 3.1 The effect of space flight on weight-bearing bones of rats (49)
  - 3.1.1 Description of experimental material (49)
  - 3.1.2 Restructuring of bone tissue (50)
  - 3.1.3 State of the organic and mineral components
  - 3.1.4 Mechanical properties of bone tissue (65)
  - 3.1.5 Use of artificial gravity to prevent bone changes in weightlessness (76)
  - 3.1.6 The effect of space flight on the non-weight-bearing bones of rats (79)
- 3.2 The effect of space flight on the skeleton of tortoises (82)

Chapter 4 Bone changes when gravitational loading is eliminated (910)

- 4.1 Experiments on rats (91)
- 4.2 Experiments on dogs (97)
- 4.3 Experiments on primates (109)

## **MUSCULOSKELETAL SYSTEM**

### **Chapter 5 Bone changes in limited motor activity (115)**

**5.1 Research on rats (116)**

**5.2 Research on dogs (97)**

**5.3 Status of the non-weight-bearing bones (131)**

**Conclusion (133)**

### **Chapter 6 Bone changes in humans in bedrest and weightlessness (136)**

**6.1 The human skeleton under conditions of bedrest and weightlessness (136)**

**6.2 Bone changes when functional loading of the skeleton is reduced from the standpoint of rapidly and slowly developing osteoporosis (140)**

**6.3 General principles underlying bone changes under conditions of weightlessness and simulations (150)**

**Conclusion (16)**

**References (172)**

## PAPER:

P1170(26/90) Shlyk GG, Rotenberg MA, Shirvinskaya MA, Korol'kov VI, Magedov VS.  
***Characteristics of nocturnal sleep in monkeys on the ground and during space flight on COSMOS-1667.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 12-17: 1989.

[12 references; 9 in English]

Neurophysiology, Sleep

Monkeys

Space Flight, COSMOS-1667

**Abstract:** Structure of sleep was studied in two monkeys, Verny and Gordy, during flight on COSMOS-1667 and in a subsequent control condition. The control condition was run in a biosatellite mock-up in which all flight experiment conditions (restraint, feeding schedule, etc.) with the exception of weightlessness were reproduced. Duration of both the flight and the control conditions was 7 days. The monkeys had undergone a 1-year training program involving development of conditioned reflexes, and habituation to rigid restraint, isolation, and the Biosprimat capsule. During the preflight period, electrodes were implanted for EEG, EOG, and EMG. Analysis of the structure of sleep utilized the standard international taxonomy. During flight, "days" in space were identical to normal ones, with illumination conditions being correlated with Moscow time. In the control condition, video recordings were made of the animals for 5 minutes every 2 hours during the day and in the flight condition, whenever the biosatellite was above the USSR.

In Verny, the greatest disruption of sleep structure was noted the night before the flight, which contained the longest period of nocturnal wakefulness, the highest number of awakenings, the longest period of superficial stage I sleep, and the shortest delta sleep period. Ratio of REM sleep to delta sleep was very high (38). This result is likely to be associated with stress engendered by final preparations for flight. The second night (the first in space) there appeared to be a "recoil" with the longest period of delta sleep observed, and reduced durations of stage I and II sleep. On subsequent nights, parameters gradually stabilized, with ratio of REM sleep to delta sleep remaining low. During the control condition, REM to delta sleep ratio remained stable and low and duration of delta sleep was relatively high. However, duration of REM sleep was rather high, which is also characteristic of neurotic humans. In the second animal, Gordy, the greatest effects (deficit of delta sleep, high ratio of REM to delta, and longest duration of nocturnal wakefulness) were also noted on the night before the flight. No recoil effect was noted on the first night in space. Throughout both conditions, delta sleep was of markedly shorter duration than in Verny; furthermore it decreased by a higher percentage in response to stress. Ratio of REM to delta sleep was very high on the first night in space. Adaptation required a longer period, 3 days, in this animal.

The authors draw the following conclusions: 1) the structure of sleep revealed that the greatest stress response occurred on the night before flight; 2) adaptation to flight conditions initially is accompanied by an increase in the proportion of REM sleep and a high ratio of REM to delta sleep; 3) there were major differences in the two monkeys studied in relative amount of delta sleep both in control and flight conditions.

Table 1: Sleep parameters in Verny during flight

Table 2: Sleep parameters in Verny in the control condition

Table 3: Sleep parameters in Gordy during flight

Table 4: Sleep parameters in Gordy in the control condition

P1171(26/90) Lychakov DV, Pashchin AN, Boyadzhieva-Mikhaylova A, Khristov I. (Latter two are Bulgarian)

***A study of the structure of the receptor organs of the vestibular apparatus in rats after flight on COSMOS-1667.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 17-26: 1989.

[43 references; 25 in English]

Neurophysiology, Vestibular System; Morphology; Receptor Organs

Rats, Male

Space Flight, COSMOS-1667

**Abstract:** Subjects in this experiment were male rats flown on COSMOS-1667 for 7 days. As a control, seven matched rats were maintained under vivarium conditions. Postflight body weight was virtually identical for the two groups. Animals were sacrificed between 4 and 8 hours after satellite landing and the left and right labyrinths were fixed between 4 and 10 minutes after sacrifice. The otolith membrane was isolated on day 4-5 after fixation and was examined with a scanning electron microscope. The utricle, saccule, and ampullae of the semicircular canals were dehydrated and serial sections 5 and 10  $\mu$ m thick prepared. All sections were examined under a light microscope and photographed. A total of 29 receptor organs were studied for the experimental group and 21 for the control. To evaluate quantitatively the extent of structural inhomogeneity, the maculae and cristae were reconstructed for a total of seven organs for the experimental and nine for the control group. To assess edema of the calyciform nerve endings in the area of the strioles in the utricle, their size was compared to that of the corresponding cells in the control group. After examination with a light microscope, some of the sections were examined with a transmission electron microscope.

The experimental animal killed first (4 hours, 22 minutes after landing) displayed a marked asymmetry in the calyciform nerve endings; those in the three cristae of the right labyrinth were swollen throughout the receptor epithelium. Such swellings were not observed in the left vestibular organ, or in the utricle or saccule of the right labyrinth; nor were they found in control animals or flight animals sacrificed later. The authors conclude that this phenomenon resulted from space flight factors, but that the change was reversible, disappearing during readaptation. No systematic differences between flight and control animals were noted, not even differences observed after previous COSMOS flights.

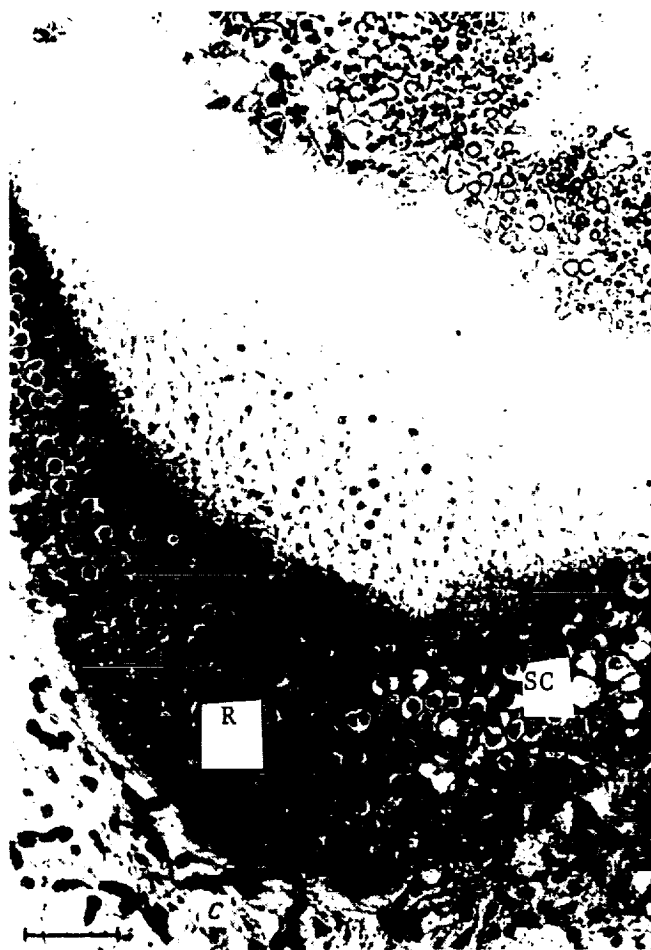
Table 1: Temporal parameters for obtaining experimental material from rats flown on COSMOS-1667

Table 2: Proportion of the area (in %) occupied by the calyciform nerve endings with respect to the cell+calyciform nerve ending complex in the striole of the utricular macula

Rat #	Control		Flight	
	right labyrinth	left labyrinth	right labyrinth	left labyrinth
1	--	73.3 $\pm$ 3.8(23)	72.1 $\pm$ 6.5(37)	--
2	--	78.5 $\pm$ 6.5(39)	79.5 $\pm$ 4.5(23)	74.0 $\pm$ 6.2(28)
3	77.0 $\pm$ 9.5(33)	--	71.3 $\pm$ 9.7(25)	--
5	77.3 $\pm$ 7.4(35)	--	--	--
6	76.7 $\pm$ 4.5(19)	--	--	--
7	74.2 $\pm$ 5.0(10)	--	--	--
Mean	76.2 $\pm$ 2.0(6)		74.2 $\pm$ 3.7(3)	

Note: For each rat the number in parenthesis refers to the number of calyciform nerve endings measured; for the average value this number refers to number of animals used.

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1.

Figure 1: Light microphotograph of a section of the utricle of a flight rat. The section was made parallel to the surface of the macula. Because of the calyciform shape of the macula, the section contains only a portion of the receptor cells. R - receptor epithelium; C - connective tissue; SC - swollen calyciform nerve endings. Scale 50  $\mu$ m



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2.

Figure 2: Light optic microphotograph of sections of the cristae of the anterior canals of the left (a, b) and right (c) labyrinths of flight rat #1

a,b - the sections were made parallel to the base of the crista; a - closer to the base; b - at the top of the crista; swollen calyciform nerve endings are located on the top of the crista; c - section was made along the crista at a slight angle. Because of this both the central and peripheral areas of the receptor epithelium are contained in the section. All calyciform nerve endings are highly swollen. SC - swollen calyciform nerve endings; C - central, P - peripheral areas of the receptor epithelium; N - a strip of nonreceptor epithelium

P1192(26/90)\* Korolev AB.

***Study of the pathogenesis of the neurological form of decompression sickness in rabbits.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 92-93;1989.

[9 references; 6 in English]

Neurophysiology, Pathogenesis; Brain

Rabbits

Decompression Sickness

**Abstract:** This work studied the pathogenic effects of experimentally induced decompression sickness on the central nervous system, in particular, the possibility of primary gas formation in the veins of the brain. The study used direct visual observation of the blood vessels of the temporal lobe of the cerebral cortex of nonanesthetized rabbits through a transparent plate of shock-resistant polystyrene implanted in the bone of the skull 5-7 days before the experiment. Throughout the experiment, the activity visible through this plate was recorded on videotape, at the same time EKG and respiration rate were recorded. Three experiments were conducted, each using 10 rabbits. In the barochamber the animals descended to an equivalent depth of 11 atm, where they remained for 60, 40, and 30 minutes, in the three experiments. In all experiments they breathed air. Duration of compression to 11 atm and return compression to 1 atm were 5 and 4 minutes, respectively. The animals were observed at 1 atm. until they stopped breathing, after which therapeutic recompression was performed.

Regardless of the length of time the animals spent under increased pressure, the same types of changes occurred in the circulation of blood and cerebrospinal fluid and in the respiratory and cardiovascular system. Immediately after decompression, there were venous and arterial spasms of the cerebral cortex. Gas bubbles in the cerebrospinal fluid and vasculature always formed after and not during decompression, first in cerebrospinal fluid and then in the veins. Gas bubbles were first observed in the walls of the vessel; subsequently they either burst and entered the venous sinuses along with blood, or they induced a spasm in the vein leading to a thrombosis and disruption of intracranial hemodynamics. The bubbles entering the venous sinus rapidly dissipated along with blood. Rate of gas formation gradually increased, drastically so after breathing stopped. No embolisms were noted in the cerebral arteries. Cardiorespiratory changes occurred later than spasms of brain vessels and gas formation in cerebrospinal fluid and brain vasculature. Soon after the appearance of gas bubbles in the veins and sinuses of the brain, breathing rate increased sharply and ultimately stopped. Characteristic EKG changes included increased heart rate, development of infarction-like QRST complexes, NS ventricular fibrillation, followed by infrequent ectopic rhythms immediately after breathing stopped. Recompression was never clinically effective, although it led to a rapid decrease in bubbles in the veins and cerebrospinal fluid. The author considers the changes observed in the brain critical to understanding of the pathogenesis of the effects of decompression on the nervous system.

P1198(26/90) Ivanov AV.

***Change in reflexive vestibular activity in response to orthostatic loading.***

Vestnik Otorinolaringologii.

1989(4): 16-19.

[15 references; none in English]

Author's Affiliation: Belorussian Research Institute on Neurology, Neurosurgery and Physiotherapy, Minsk

Neurophysiology, Vestibular Activity

Humans, Males

Orthostatic Loading, Stand Test, Tilt Test

**Abstract:** Vestibular excitability was studied nystagmographically in 19 healthy men during stand and tilt tests. The vestibular system was stimulated using monothermic caloric irrigation. Reflex vestibular nystagmus was recorded with the eyes closed. Mean values of ENG parameters (latent period, number of nystagmic beats, frequency and duration of nystagmus, and amplitude and rate of the slow phase) were compared in prone position and during active and passive (stand and tilt) orthostatic tests.

When subjects were standing, most nystagmic parameters tended to decrease, while latent period increased and frequency increased to a nonsignificant extent, suggesting decreased excitability of the vestibular system. When three subjects were placed in an upright position on a tilt table, inhibition of nystagmus was a great deal more pronounced than in active standing position.

Table 1: Changes in the major parameters of reflexive nystagmus in stimulation of the right otolith during a stand test

Table 2: Changes in the major parameters of reflexive nystagmus in stimulation of the right otolith during a tilt test

Figure: Diagram of the tilt test

## PAPERS:

P1188(26/90) Arustamov OV, Khaydakov MS.

***The effect of increased consumption of vegetable protein on calcium metabolism in rats undergoing hypokinesia.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 85-86; 1989.

[5 references; 4 in English].

Metabolism, Calcium

Rats, Males

Nutrition, Vegetable Protein; Hypokinesia; Tail Suspension

**Abstract:** In this study an unspecified number of male Wistar rats were divided into four groups on the basis of diet: group A was fed a ration which had casein (18%) as its protein source; rats in the next three groups, B1, B2, and B3, received a diet in which the primarily protein source was soy (18, 27, and 36%, respectively). All diets contained 0.6 and 0.3% calcium and phosphorus, respectively. The diets containing soy protein were supplemented with a solution of ergocalciferol (20 ME per rat). Water consumption was not limited. Half of the subjects in each group were subjected to tail suspension for 35 days. The animals were weighed regularly and Ca balance studied. After treatment they were sacrificed and concentrations of Ca, inorganic P, 25-hydroxy-vitamin D, parathyroid hormone, and activity of acid and alkaline phosphatase were measured in blood serum. Active Ca transport in the intestine was estimated on the basis of accumulation of  $^{45}\text{Ca}$  in an isolated section of the small intestine using the disk method.

During the experiment, non-suspended group A animals gained weight at a rate of 0.4% per day. The soy ration was associated with weight maintenance, and in the case of the highest level, weight gain in non-suspended animals. The soy groups displayed an increase in 25(OH)D by 208, 254, and 259%, for groups B1-3, respectively and a slight increase in parathyroid hormone (by 11-12%). Alkaline phosphatase activity decreased by 32% in animals receiving the most soy protein, acid phosphatase activity decreased by 28% in group B1, but was at control level for B3. The animals receiving the smallest amount of soy protein showed increased (by 26.5%) Ca transport in the intestine. Transport rate decreased as amount of soy protein increased. Concentrations of Ca and inorganic P remained at control level in the soy groups, while renal excretion of Ca drastically (by a factor of 20-25) decreased starting during the first days of the experiment and continuing until its termination.

Tail suspension of animals receiving casein was associated with an 8.7% decrease in weight, followed by a return to baseline value. Blood levels of Ca and parathyroid hormone increased insignificantly, while phosphatase activity decreased. Other blood parameters were comparable to control. Renal excretion of Ca doubled and its absorption in the small intestine exceeded control level by 100.4%. Animals fed 18% soy protein and suspended lost 14.2% of body weight. When the amount of protein was increased, weight loss did not occur in experimental animals. Compared to control animals receiving casein, suspended group B animals displayed elevated levels of parathyroid hormone and intestinal Ca absorption, with concentration of 25(OH)D elevated by 208, 264, and 205% in the three groups. Blood calcium did not differ from control while inorganic phosphorus increased substantially in group B1 only. In the B groups, alkaline phosphatase activity tended to increase, while that of acid phosphatase decreased in all groups. Renal excretion of Ca increased by a factor of 10-12.

The authors conclude that the changes occurring in the rats on a vegetarian diet reflect a new functional level of the Ca-regulation system which supports a normal level of Ca in blood,

## **NUTRITION**

despite increased excretion. The effect of the diet on Ca homeostasis in suspended rats was less significant, since the suspension itself increased levels of parathyroid hormone and Ca absorption to maximal values, masking the effect of the diet.

P1197(26/90) Klimovich VV, Lukashik NK.

***Thiamin metabolism in rats with a B<sub>1</sub> deficiency exposed to hypokinesia.***

Voprosy Pitaniya.

1989(4): 62-65.

[18 references; 6 in English]

Authors' Affiliation: Grodensk Medical Institute.

Metabolism, Thiamine

Rats, Male

Nutrition, B<sub>1</sub> Deficiency; Hypokinesia; Immobilization Cages

**Abstract:** An experiment was performed on a total of 32 outbred male rats. A control group was maintained individually in spacious cages, while experimental animals spent 15 days in immobilization cages. Vitamin B<sub>1</sub> deficit was created in half the animals in each group by introducing the B<sub>1</sub> antivitamin oxythiamin into the drinking water in a dose of 2 mg per kg per day throughout the experiment. The animals were fed ordinary laboratory rations. After 15 days had elapsed, the animals were sacrificed. Activity of transketolase (TK) was measured in whole blood, various age populations of erythrocytes, and homogenates of the liver and gastrocnemius muscle. Packed red cells with plasma and leukocytes removed were fractionated into old, mature, and young erythrocytes using the method of serial osmotic hemolysis. Thiamidiphosphate (TDP) (50 µg) was introduced to a sample of hemolysate of young cells to measure the TDP effect. Activity of pyruvate dehydrogenases (PDH) and α-ketoglutarate dehydrogenase (KFD) was measured in liver and gastrocnemius muscle homogenates, the concentration of TDP, the co-enzyme form of the vitamin, and protein were also assessed.

Vitamin B<sub>1</sub> deficit reduced the concentration of TDP in the liver and left it unaltered in the gastrocnemius muscle. Concentration of TDP increased in the liver of vitamin deprived animals if they were exposed to hypokinesia. TK activity decreased in whole blood in vitamin-deficient animals and to an even greater extent in hypokinetic animals. Immobilization had no effect on mature or old erythrocytes. TK activity in young erythrocytes was depressed when vitamin deficiency was combined with hypokinesia. Activity of TK and KFD was depressed in the liver of vitamin deficient animals. Introduction of oxythiamin for 15 days did not affect PDH activity. In the gastrocnemius muscle no differences were found in the activity of TK. In rats with normal vitamin levels, hypokinesia was associated with increased PDH activity. Activity of KDH in the muscles was reduced in vitamin deficient rats exposed to hypokinesia.

The authors conclude that limiting movement substantially increases the severity of vitamin deficiency, leading to disruption of utilization of co-enzyme forms of thiamin and more severe inhibition of vitamin-dependent enzymes (TK, α-KDH).

Table 1: Activity of TK in whole blood and erythrocyte fractions in rats after a 15-day period of hypokinesia and vitamin deficiency induced by oxythiamin

Table 2: Activity of TK, PDH, and α-KDH in the liver of rats after a 15-day period of hypokinesia and vitamin deficiency induced by oxythiamin

Table 3: Activity of TK, PDH, and α-KDH in the muscles of rats after a 15-day period of hypokinesia and vitamin deficiency induced by oxythiamin

Table 4: Concentration of TDP in tissue of the liver and gastrocnemius muscle in rats after a 15-day period of hypokinesia and vitamin deficiency induced by oxythiamin

## MONOGRAPH:

M159(26/90) Kovalenko PA.

Prostranstvennaya oriyentirovka pilotov: Psikhologicheskie osobennosti

Пространственная ориентировка пилотов: Психологические особенности

[*Spatial orientation of pilots: Psychological Characteristics*]

Moscow: Transport; 1989.

[231 pages; 65 tables; 28 figures; 132 references; 18 in English]

**Key Words:** Perception; Spatial Orientation; Psychology; Aviation Medicine; Human Performance; Humans, Pilots; Pilot Training

**Annotation:** This monograph considers the problem of teaching pilots an effective spatial orientation technique, one that permits them to determine their spatial position correctly and rapidly in visual and instrument flight with various types of artificial horizon. A comprehensive approach to solving this problem is developed, various orientation techniques are described for the first time, and the structure of the pilots' mental operations and representations of the spatial position of the aircraft are considered. This book is intended for pilots, instructors, and teachers in flight training schools and may also be useful to psychologists and specialists in ergonomics.

## CONTENTS

### Foreword (3)

### Chapter 1 Spatial orientation (background) (7)

- 1.1 Basic conceptions regarding spatial orientation in pilots(7)
- 1.2 Psychological characteristics of orientation in roll and pitch (14)
- 1.3 Use of imagery theory to select representation mode for roll and pitch (29)
- 1.4 Existing approaches to teaching pilots spatial orientation (45)

### Chapter 2 Approach, research methodology and instruction (50)

- 2.1 Justification for the approach (50)
- 2.2 Research methodology (72)
- 2.3 Methodology for teaching pilots effective spatial orientation techniques (78)

### Chapter 3 Spatial orientation in visual flight (83)

- 3.1 The need for visual flight (83)
- 3.2 Description of the represented object (85)
- 3.3 Usability of environmental cues in orientation (90)
- 3.4 Spatial orientation techniques (93)
- 3.5 Stability and efficiency of spatial orientation techniques (99)
- 3.6 Contents of the image and internal operations in various spatial orientation techniques (109)
- 3.7 Discussion of results (116)

### Chapter 4 Spatial orientation in instrument flight and during the transition from visual to instrument flight and vice versa (126)

- 4.1 Description of the object represented (126)
- 4.2 Characteristics of pilot performance with artificial horizons with various modes of representing pitch and roll (129)
- 4.3 Usability of qualitative and quantitative roll units in instrument flight(138)
- 4.4 Taxonomy of spatial orientation techniques in instrument flight (141)

## **PERCEPTION**

- 4.5 Efficacy of spatial orientation techniques (147)**
- 4.6 Subject matter and mental operations in instrument flight (149)**
- 4.7 Characteristics of transition from visual to instrument flight and vice versa (152)**
- 4.8 Discussion of results (158)**

### **Chapter 5 Manipulative capacity of the visual systems of pilots (169)**

- 5.1 Manipulative capacity -- the basis for spatial orientation (169)**
- 5.2 Description of the new "Artificial Horizon" test (172)**
- 5.3 Experimental validation of the "Artificial Horizon" test (175)**

### **Chapter 6 Composition of working and permanent conceptual models of pilots (196)**

- 6.1 Description of the potential structure of conceptual models(196)**
- 6.2 Conceptual models in visual and instrument flight (200)**
- 6.3 Discussion of results (212)**

### **Conclusion (219)**

### **References (223)**



**MONOGRAPH:**

M154(26/90) Berezin FB.

Psikhicheskaya i Psikhofiziologicheskaya Adaptatsiya Cheloveka; Психическая и  
Психофизиологическая Адаптация Человека;

[*Psychological and Psychophysiological Adaptation in Humans*]

Leningrad: Nauka; 1988.

[270 pages; 36 Tables; 34 Figures; 237 References; 110 in English]

Affiliation: Institute of Biological Problems of the North; USSR Academy of Sciences; Far  
Eastern Division

Psychology, Stress; Human Performance

Humans

Adaptation

Annotation: This monograph is devoted to psychological adaptation -- one of the fundamental processes determining whether humans will develop an appropriate relationship with their environment and whether the psychological process responsible for behavior will be coordinated with the physiological mechanisms that must support that behavior. The author describes the major aspects of psychological adaptation. The roles of emotional stress, anxiety, frustration, and factors supporting resistance to stress are described. On the basis of data concerning autonomic and humoral regulation under conditions of varying degrees and types of psychological adaptation, the author analyzes psychophysiological relationships, the system that regulates them, and their multivariate psychophysiological characteristics. Psychological adaptation and psychophysiological relationships are considered as they relate to changes in the man-environment system. The association between psychological adaptation and successful job performance is demonstrated, and the role played by disrupted psychological adaptation in development of certain pathological states is discussed.

**CONTENTS**

Introduction (3)

Anxiety and adaptive mechanisms (8)

The problem of adaptation and emotional stress (8)

Psychological adaptation and anxiety (13)

Mechanisms of psychological adaptation (41)

Certain aspects of the organization of emotional stress and stress resistance (71)

Frustration and the stress it engenders (71)

Psychological conflict (82)

Integration of behavior (89)

The correlations between frustration stress and behavior integration (97)

Frustration threshold (103)

Frustration intolerance and lability (118)

Achievement motivation (118)

The relationship between anxiety and psychological adaptation during the process of  
adaptation (124)

The significance of microsocial interactions, and the population and occupational aspects of adaptation (131)

Psychological adaptation and microsocial interaction (131)

Adaptation in individuals and populations (143)

Psychological adaptation and job performance (156)

Psychological adaptation and the structure of psychophysiological relationships (183)

Psychophysiological relationships under conditions of significant changes in the man-environment system (183)

Psychophysiological aspects of autonomic regulation and cerebral activation (186)

Psychophysiological relationships and the humoral regulation system (208)

Multilevel structure of psychophysiological relationships (225)

Complex psychophysiological characteristics (225)

The functional system for regulating psychophysiological relationships (231)

Psychophysiological relationships in somatic illnesses and the psychosomatic continuum (236)

Conclusion (248)

Abbreviations (2598)

References (260)

## RADIOBIOLOGY

### PAPERS:

P1191(26/90)\* Cherkasov GV.

***Acid tolerance of erythrocytes exposed to constant magnetic fields varying in rate of induction increase.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 90-92; 1989.

[15 references; none in English]

Hematology, Erythrocytes, Acid Tolerance

Rats, Male

Radiobiology, Magnetic Field, Induction Increase Rate

**Abstract:** The goal of this work was to investigate the effects of rate of increase in magnetic inductance on acid tolerance of erythrocytes. A total of 83 outbred male rats were exposed to a constant magnetic field of 0.4 T. Mean rate of inductance increase was 2 and 8 mT/sec. A special device was constructed to obtain different rates of inductance increase. Biological material consisted of blood samples taken from the tail vein of rats and added to 5 ml of normal saline. Samples were placed in a thermostatic cell (24°) and exposed to the constant magnetic current (rate of inductance increase 2, 4, and 8 mT/sec.) or placed outside of it. In a second study, blood of rats was examined before and after animals' exposure to the magnetic field. Acid tolerance of erythrocytes was evaluated using an undescribed method.

In the *in vitro* experiment, reliable changes were found only in the group of highly-stable erythrocytes. At 8 mT/sec. the number of these cells decreased to 53.4%, at 4 mT/sec. to 74.9%, and at 2 mT/sec. to 86.5%. This effect was only statistically significant for the highest inductance increase rate. Similar results were obtained in the *in vivo* study, but it was found that the effect only occurred in animals with a relatively high proportion of young erythrocytes. The effect persisted for only 30 minutes.

The author concludes that only increase and decrease of induction of a magnetic field when the electromagnet is turned on and off can lead to alterations in erythrocyte membranes of rats. These changes involve decreased resistance to hemolysis and are a direct function of rate of inductance increase.

Table 1: Concentration of highly resistant erythrocytes at various rates of inductance increase of a magnetic field of 0.4 T in *in vitro* and *in vivo* experiments

Table 2: Concentration of high-tolerance erythrocyte in "sensitive" and "tolerant" rats at an inductance increase rate of 8mT/sec.

P1199(26/90) Tabukashvili RI, Ushakov IB.

***Certain biochemical mechanisms underlying the combined effects of extreme factors.***

Voprosy Meditsinskoy Khimii.

35(4): 111-114; 1989.

[15 references; 1 in English]

Authors' Affiliation: Tblisi Medical Institute

Radiobiology, Ionizing Radiation, Liver

Rats, Males

Hypoxia, Microwave Radiation, Radioprotective Effects

**Abstract:** If a biological subject is exposed to certain factors (e.g., exogenous hypoxia, acceleration, vibration, and microwave radiation) before irradiation with ionizing radiation, these factors have a radioprotective effect. The biochemical mechanisms of these effects have not been studied. The objective of this work was to investigate the possibility of the existence of a biochemical substance that forms in response to exposure to stressors and provides protection against radiation. Experiments were performed on outbred male rats. In individual cages the animals breathed a gas mixture containing 5% oxygen in nitrogen for 8 minutes. Irradiation with microwaves (2.45 GHz, power density- 100 mW/cm<sup>2</sup>) also lasted 8 minutes. Irradiation treatment utilized  $\gamma$ -rays to a dose of 8.5 Gy and dose rate of 70 cGy/min. Acid proteolytic activity was measured in liver tissue homogenate that was centrifuged and then divided into two parts. Nonionic detergent was added to one portion for subsequent measurement of enzyme activity, and the other portion was further centrifuged to produce a supernatant for measurement of free activity of acid peptide hydrolase. A total of 14 experimental groups were used. In condition 1 rats were exposed only to  $\gamma$ -irradiation. In condition 2 rats were exposed to hypoxia immediately followed by irradiation. In condition 3 rats were irradiated 15 minutes after intraperitoneal introduction of liver extract prepared immediately after donors were exposed to hypoxia. In condition 4 irradiation occurred 15 minutes after exposure to microwave radiation. In condition 5 irradiation occurred 15 minutes after injection with blood serum obtained immediately after donor had been exposed to hypoxia. In condition 6, rats were irradiated and then given liver extract of donors which had been given auranofin (colloidal gold) and after 24 hours exposed to hypoxia. In condition 7 rats were given auranofin (25 mg/kg) and then irradiated after 24 hours. The next groups of subjects were subjected to hypoxia and then liver extracts were prepared and precipitated with 10% TXU (??) (condition 8) or 20% sulfosalicylic acid (condition 9). The supernatants were collected and after dialysis against distilled water injected in rats subjected to irradiation. Animals of group 10 were irradiated and then injected with liver extracts obtained from animals subjected to hypoxia. In conditions 11 and 12 subjects were not treated, but their livers were used to produce extracts, which were injected in recipients before and after irradiation. Animals in condition 13 were injected with auranofin, and after 24 hours acid proteolytic activity of peptide hydrolase was measured in the liver. In condition 14, acid proteolytic activity was measured after rats were exposed to hypoxia.

The radioprotective effect of breathing a hypoxic mixture and of being injected with liver extract from donors that had been exposed to hypoxia were approximately the same. This suggests the production of a biologically active substance. Liver extracts from animals exposed to microwave irradiation were also radioprotective. Blood serum from animals exposed to hypoxia did not have this effect. When liver extract was prepared from animals given auranofin before exposure to hypoxia, there was no radioprotective effect. Direct administration of auranofin inhibited acid proteolytic activity and decreased longevity of irradiated animals compared to animals irradiated without auranofin. This is interpreted as meaning that loading of the lysosome apparatus of the liver with colloidal gold before hypoxia eliminates the

## RADIOBIOLOGY

radioprotective effect of liver extract. When liver extracts were prepared from animals exposed to hypoxia with the proteins and peptides precipitated out (conditions 8 and 9), no protective effects were found. Thus the protective factor must be found in the protein or oligopeptide fraction.

The authors conclude that exposure to the first extreme factor (hypoxia, microwave radiation) triggers the formation of biochemically active polypeptide substances in the cell, which through the system of cell receptors affect various stages of metabolism, increasing the body's defense responses against ionizing radiation.

Table: Survival of animals after  $\gamma$ -irradiation with preliminary introduction of liver extract and blood serum of rats subjected to the effects of a hypoxic medium and microwave radiation

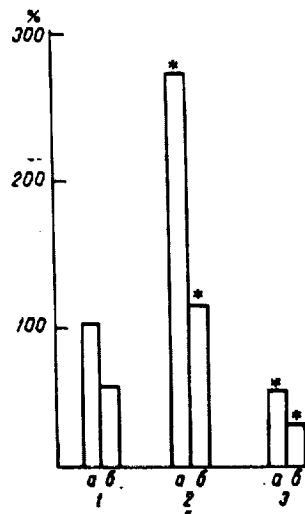


Figure: Acid proteolytic activity in the livers of rats after exposure to hypoxia and auranofin  
Abcissa: 1 - control; 2 - immediately after exposure to hypoxia; 3 - 24 hours after intraperitoneal introduction of auranofin in a dose of 25 mg/kg; a - total activity; b - free activity. Ordinate: activity (in % control); \*  $p < 0.05$  relative to control.

## RADIOBIOLOGY

P1201(26/90)Tabukashvili RI, Ushakov IB.

***Possible mechanisms of the radiomodifying effect of exogenous hypoxia on microwave radiation.***

Radiologiya.29(4): 529-532; 1989.

[14 references; 1 in English]

Authors affiliation: Tblisi Medical Institute.

Radiobiology, Ionizing Radiation, Liver

Rats, Males

Hypoxia, Microwave Radiation, Radioprotective Effects

**Abstract:** The objective of this work was to elucidate certain possible biochemical mechanisms of the radioprotective effect of exogenous hypoxia and microwave radiation. Experiments were performed on 11 male rats. Exposure to hypoxia occurred in individual cages through which hypoxic (5% oxygen in nitrogen) gas was piped at 20 l/min. for 8 minutes. Microwave radiation had a frequency of 2.45 GHz, power density of 100 mW/cm<sup>2</sup> and lasted 8 minutes. This microwave exposure corresponded to 0.1% probability of fatality.  $\gamma$ -irradiation utilized <sup>60</sup>Co as a source, with a dose of 8.5 Gy and dose/rate of 79.3 cGy/min. The experiment had 8 conditions. Condition 1 involved only  $\gamma$ -irradiation. In condition 2 animals were irradiated immediately after exposure to hypoxia. In the other conditions animals were injected with liver extract obtained by centrifugation of liver homogenates of donor rats. In condition 3 rats were irradiated after injection of liver extract from donors exposed to hypoxia. In condition 4 rats were irradiated 15 minutes after injection of extract from donors exposed to microwave radiation. In condition 5, liver extract from rats exposed to hypoxia was injected after radiation. In condition 6 rats were irradiated after and in condition 7 before injection of liver extract from untreated rats. In condition 8 rats were irradiated 15 minutes after injection of blood serum obtained from rats exposed to hypoxia. The radiomodifying effect was estimated from mean survival time and survival rate of experimental animals over a period of 30 days.

A slight and comparable radioprotective effect was observed in animals exposed to hypoxia before irradiation and those injected before irradiation with liver extract from rats exposed to hypoxia. Liver extract of rats exposed to microwaves also had a protective effect when injected before irradiation. Since blood serum injection did not have a protective effect, the authors conclude that the biologically active substances is most likely to operate at the cellular level. Data indicating that when liver extracts from rats exposed to hypoxia are injected in recipients after they have been irradiated there is no radioprotective effect, are interpreted as supporting the theory that the radioprotective effect is achieved by inhibiting the cellular cycle of radiosensitive tissues and thus decreasing number of mitoses. The authors hypothesize that due to exposure to the first extreme factor (hypoxia or microwave radiation) biologically active substances may form in the cells and bind with internal or external receptor cells to immediately alter the rate of cellular metabolism. Subsequently, the number of mitoses decreases in the initial few hours, and this increases the body's resistance. Some time later, synthesis of nucleic acids increases, enhancing reparative processes in the irradiated individual.

**Table:** Survival rate of animals and mean survival time after  $\gamma$ -irradiation and injection with liver extract or blood serum from donor rats exposed to hypoxia or microwave irradiation

# RADIOBIOLOGY

## MONOGRAPH:

M153(26/90) Antipov VV (Editor)

Biofizicheskiye Osnovy Deystviya Kosmicheskoy Radiatsii i Izlucheniya Uskoriteley;  
Биофизические Основы Действия Космической Радиации и Излучений  
Ускорителей

*[The Biophysical Bases for the Effects of Cosmic Radiation and Radiation from Accelerators.]*

Volume 60 In series: Problemy Kosmicheskoy Biologii,  
Leningrad: Nauka; 1989.

[255 pages; 32 Tables; 70 Figures; 327 references; 114 in English]

Key Words: Radiobiology; Cosmic Radiation, Accelerators; Biophysics; Biological Effects;  
Hadrons

Annotation: This monograph summarizes and draws conclusions from the results of numerous investigations, mainly by Soviet researchers, describing the action of high energy cosmic radiation and its simulations using accelerators of heavy ions, and also their biological effects. This is the first systematic review of research material devoted to the specific effects of hadrons. The authors cite facts indicating that these particles have the capacity to induce severe local destruction of tissue and organs, making them one of the major factors limiting the duration of space flights. Results of investigation of the biological effects of multicharged ions and protons are presented and the kinetic model of radiation damage is described. This model is based on microdosimetric concepts and explains observed changes in the dose-survival curve as LET and dose rate increase.

## CONTENTS

Foreword (I.G. Akoyev, V.A. Sakovich) (5)

### PART I BIOLOGICAL EFFECTS OF SUPERHARD COSMIC RADIATION: THEIR BIOPHYSICAL INTERPRETATION

Chapter 1: Analysis of the results of biological experiments in space (I.G. Akoyev, S.S. Yurov)

General analysis of experimental results (7)

The local radiation factor in space (11)

Testing of the hadron hypothesis (19)

The effects of weightlessness and radiation (21)

Chapter 2: Physical characteristics of the nuclear active component of cosmic radiation

(G.B. Zhdanov) (24)

The energy spectrum and composition of primary high-energy cosmic radiation (26)

Multiple generation of particles using super-high energy nucleons and nuclei (28)

Development of electron-photon showers within nucleon-nucleus cascades (36)

Ways to simulate radiobiological effects (430)

Chapter 3: Simulation of the superhard component of cosmic radiation using the Serpukhov accelerator (V.G. Golovanchik, V. N. Lebedev, M.S. Maslov) (45)

Characteristics of the mixed radiation field of the Serpukhov accelerator (45)

Characteristics of the radiation field in a beam of high energy neutrons (50)

Formation of radiation fields in a tissue-equivalent phantom using high energy particles  
(55)

The problem of low doses and evaluation of RBE of secondary radiation (57)

Interpretation of the results of radiobiological accelerator experiments (58)

## **RADIOBIOLOGY**

**Chapter 4: Biological effects of high energy hadrons in accelerator experiments (I.G. Akoyev, S.S. Yurov) (60)**  
Investigations using the Serpukhov accelerator (61)  
Biological effects with other accelerators (76)

**Chapter 5: Microdosimetric analysis of radiation-induced effects (V.I. Ivanov, I.M. Dmitriyevskiy) (80)**  
The concepts of microdosimetry (80)  
The observed dispersion of effect (82)  
The relationship between radiation-induced effect and dose (83)  
Analysis of the variability of radiobiological effects in experiments with high-energy radiation (84)

**Chapter 6: Biophysical interpretation of hadron effects (I.G. Akoyev, S. S. Yurov, V.I. Ivanov) (88)**  
RBE and mean LET values of radiation (88)  
General analysis of the results of accelerator experiments (94)  
The scope of the RBE-LET function (96)  
The physical bases of hadron effects (98)  
The significance of research on hadron effects (105)

### **PART II: CHARACTERISTICS OF BIOLOGICAL EFFECTS AND PROPERTIES OF MULTICHARGED NUCLEAR PARTICLES AND HIGH ENERGY PROTONS ON SPACE FLIGHTS**

**Chapter 7: Properties of cosmic radiation to which spacecraft crews are exposed (109)**  
Galactic cosmic radiation (A.V. Kolomenskiy) (109)  
Basic characteristics of solar cosmic radiation (A.V. Kolomenskiy) (115)  
The Earth's radiation belts (A.V. Kolomenskiy)(118)  
Characteristics of the radiation field in space (A.V. Kolomenskiy) (122)  
Evaluation of radiation risk from solar flares during space flight (A.V.Kolomenskiy)(125)  
Dosimetric studies in low Earth orbit (V.Ye. Dudkin) (127)  
Radiation physics investigations of the components of cosmic radiation (V.V. Markelov, V.I. Red'ko, I.V. Chernykh) (136)

**Chapter 8: Simulation of the effects of cosmic radiation using ground based radiation sources and biosatellites (143)**  
On simulation of radiation effects of cosmic radiation using ground-based sources (V.I.Popov) (143)  
Formation and monitoring of a proton beam on a JINR (Joint Institute of Nuclear Research) synchrotron (M.A. Sychkov) (146)  
Creation of irradiation conditions and methods of dosimetry for accelerated multicharged ion beams (Ye.I. Kudryashov) (153)  
Characteristics of dose fields in experiments on the JINR proton synchrotron (V.I. Popov, A.I. Portman) (162)  
Simulation of radiation effects on biosatellites (R.A. Kuzin, V.A. Shafirkin, V.V. Yurgov) (167)

**Chapter 9: Biological effects of protons (N.I. Ryzhov) (170)**  
Early effects of proton irradiation (170)  
Remote effects of proton irradiation (175)



## **RADIOBIOLOGY**

- Chapter 10: Biological effects of heavy ions (N.I. Ryzhov) (178)  
    Effects of heavy ions on the simplest biological systems (178)  
    Effects of heavy ions on mammalian cells and tissue (18)  
    Radiobiological effects of heavy ions in combination with modulating agents (182)  
    Characteristics of recovery after irradiation with heavy ions (184)  
    Radiobiological effects of exposure to high-energy heavy ions (186)  
    Derivation of quality factors for heavy ions (190)
- Chapter 11: Biological effects of galactic cosmic radiation (N.I. Ryzhov) (193)
- Chapter 12: Generalized kinetic model of radiation damage to cells (A. T. Gubin, Yu.L. Minayev, V.A. Sakovich) (198)  
    Conceptual basis for the model (198)  
    Description of the model and "Bakteron" program (202)  
    Results of the analytic investigation of the model and approximation of continuous absorption of energy (207)  
    Comparison with experiment data for sparsely ionizing radiation (213)  
    Comparison with experimental data for densely ionizing radiation (219)  
    Simulation of multiple radiation damage in cells (224)
- Conclusion (V.V. Antipov) (229)
- References (232)  
List of abbreviations (249)  
Abstract (in English) (249)

### PAPERS:

P1172(26/90)\* Alpatov AM, Il'in YeA, Antipov VV, Tairbekov MG.

***Biological experiments on COSMOS-1887.***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 26-32; 1988.

[21 references; 11 in English]

Space Biology and Medicine, Biological Experiments; Metabolism, Cell; Genetics; Biological Rhythms; Developmental Biology; Cytology; Population Studies

Microbiology, *E. coli*, *Tetrahymena pyriformis*, *Wolffia*, *Haplopappus*, Guppies, Tritons, *Drosophila melanogaster*; Beetles, *Macaca mulatta*, Stick Insects

Space Flight, COSMOS-1887; Radiobiology, Cosmic Radiation; Adaptation

Abstract: The flight of biosatellite COSMOS-1887 lasted 13.5 days, from September 29, to October 12, 1987. The satellite's life support system maintained parameters at the following levels: temperature 22-25°, air pressure 725-765 mm Hg, humidity 40-65%, pO<sub>2</sub> 140-180 kPa, pCO<sub>2</sub> 2-3 kPa. Biological subjects were housed in containers communicating with the cabin atmosphere of the satellite, in the dark. Exceptions were the infusoria, which were housed in a thermally stable device, "Cytos-3" and the inhabitants of the hermetically sealed "Aquarium" device (*Chlorella*, guppies), where a diurnal schedule of illumination was adhered to. Subjects were placed in their containers and loaded on board the satellite 2 days before launch. The major ground control (synchronous) condition followed the experimental group with a 1-day time lag so that temperature conditions could be reproduced exactly on the basis of information transmitted to Earth. Additional controls were run for certain experiments to separate out the effects of certain space flight factors. The biosatellite landed in an unscheduled region, delaying removal of subjects to 1 day after landing. During the day, air temperature dropped in the cabin. The minimum temperature in the containers was 15°C. This temperature drop was reproduced in the synchronous condition. Only the fish suffered from the cold.

One experiment was performed on one-celled eucaryote organisms, the ciliate *Tetrahymena pyriformis* and the Cytos-3 device developed in France. The device maintained the cell culture at a constant temperature and periodically fixed material. Before the experiment, isolated cells were placed in plastic packets with capacity of 1.2 ml containing a nutritive substrate and ampuls with a fixative. Two flight and two control packets were loaded at the same time. Sister cells were used in the two conditions to ensure identical biomaterial. Initially the cells were maintained at 8°C; after injection into orbit the temperature was maintained at 25°, which has been established as optimal for infusoria to divide. Fixation occurred after 0, 12, 24, 36, and 48 hours in orbit. It was found that in weightlessness the organisms underwent division more rapidly, cells became more spherical in shape, and the level of protein decreased. These results agree with others obtained on another species of infusoria.

Results indicating accelerated growth and aging of *Wolffia* and increased level of lipid peroxidation by the cell membrane in a tissue culture of *Haplopappus* also demonstrated the possibility of weightlessness stimulating cellular metabolism.

A lysogenic culture of *E. coli* bacteria was used in an experiment proposed by Moscow schoolchildren to evaluate the effect of space flight factors on the procaryote cell. In an *E. coli* culture the  $\lambda$  bacteriophage is in an inactive state. Its DNA is adjusted to the gene of the host bacteria and is replicated with it. Various physical and chemical factors have the capacity to put the bacteriophage into an active state. When this occurs the host cell is destroyed and particles of the bacteriophage are emitted into the surrounding environment. On COSMOS-1887 it was

## SPACE BIOLOGY AND MEDICINE

established that bacteriophage induction increased by a factor of 3.2, which agrees with previous data and is attributed to the positive effects of radiation.

Unlike previous genetic experiments in space, studies on COSMOS-1887 were directed at evaluating the role of the genetic apparatus in the cellular response to weightlessness and in the mechanism of adaptation to this factor. One proposed mechanism of adaptive restructuring (rearrangement) in the gene is alteration of the heterochromatization of individual DNA segments, and repression-depression of whole gene blocks. To test this hypothesis, frequency of meiotic crossing over was studied in fruit flies in various locations on a single chromosome. Two strains of *Drosophila melanogaster* were used; one, a mutant, contained a chain of gene markers manifest in the phenotype. After the flight it was established that the frequency of recombinations between the genes ru-h and h-cu increased in weightlessness, while crossing over between the cu-e genes decreased. These results support the hypothesis. Other possible mechanisms underlying activation of the genome are gene amplification and polyploidization of nuclei. To evaluate the roles of these mechanisms in the response to space, a cytological study of oogenesis was conducted in fruit flies and tritons (aquatic newts). No changes were found in the egg sacs of the flies, so that the participation of polyploidization was not confirmed. However, postflight studies revealed increased number and size of nucleoli and increased diameters in the oocytes of the tritons. This suggests additional amplification of genes of rDNA under the influence of space flight factors.

Cytological research was performed on lymphocytes from the blood of *Macaca mulatta* monkeys (two flight and four control animals) pre- and postflight. The metaphases of the first and second mitoses were analyzed. Instances of chromosome destruction (breaks) were counted in the first mitosis, and sister chromatid exchange in the second mitoses. It was found that space flight factors and return to the Earth led to a decreased percentage of dividing lymphocytes in peripheral blood of monkeys. The flight animals displayed some elevation in the frequency of chromosome rearrangements and sister chromatid exchanges and a significant increase in nucleolus-forming associations. This suggests that the chromosomal apparatus may participate in adaptation to weightlessness in monkeys.

Circadian rhythms in space typically have been studied under conditions of a diurnal illumination schedule, which may mask possible effects. On COSMOS-1887 circadian rhythms were studied under conditions of darkness in darkling beetles, housed in individual cells. During 8-10 periods pre- and postflight, the insects' motor activity was recorded. After flight, seven of the eight beetles displayed a significant decrease in the period of free-running diurnal rhythms. In two subjects, the rhythm gradually returned to baseline postflight. A control experiment indicated that neither vibration nor chilling was responsible for this effect. This result is not only potentially important theoretically, but also suggests that optimal duration of "space days" may differ from that on Earth.

An experiment originally performed on Spacelab D-1 suggesting that weightlessness has a disastrous effect on embryonal development of insects was replicated on COSMOS-1887. Postflight both embryos and hatched larvae of the Indian stick insect, *Carausius morosus*, were studied. Subjects were exposed to space during different stages of development. Postflight, staggered fixation of the biomaterial provided information concerning the course of development of and compensation for the effects of space flight factors. Tracks of charged particles were detected in the insects. It appeared that embryonal development per se did not alter as a result of space flight factors, even hits by HZE particles: no anomalies or developmental delays were noted. However, postflight, there was a marked decrease in the number of larvae hatching and a reliable increase in frequency of morphological anomalies. Combined effects of weightlessness and radiation hits were also noted.

## SPACE BIOLOGY AND MEDICINE

Experiments on tissue regeneration were run on COSMOS 1887 on Spanish triton newts, replicating experiments performed on COSMOS 1667. Results confirmed earlier findings that regeneration in space proceeds normally, and is actually accelerated postflight due to increased cell proliferation in the blasteme. Additional experiment on planaria and impatiens plants verified that regeneration is normal in space.

Research on COSMOS-1887 is summarized in the table below.

Biological research for future Soviet biosatellites will have the general objectives of explicating the biological role of weightlessness as an ecological factor and evaluating the depth and nature of its effects (harmful, modifying, stimulating, facilitating) at various structural levels. Practical results will include information to support a conclusion concerning potential benefits of artificial gravity on future long-term flights, recommendations for countermeasures, and selection of species for future space ecosystems. Research will be conducted at the cellular, individual, and population levels. In cellular biology, goals include searching for gravity-dependent processes in the cells and nonspecific gravity sensors and identifying adaptive changes in the cell occurring in weightlessness, and studying their "mechanisms and biological "meanings." At the level of the individual organism, scientists will attempt to assess the nonspecific effects of weightlessness, discover how these effects vary as a function of linear dimensions (body size) and ecology, and study changes in the biological needs of organisms exposed to weightlessness for long periods (up to several generations). Population studies will help us understand how weightlessness acts as a natural selection factor to influence the direction and rate of the process of microevolution.

## SPACE BIOLOGY AND MEDICINE

The major results of biological experiments on COSMOS-1887

Subjects	Parameter	Effects of Space Flight	Authors
Lysogenic culture of <i>E. coli</i>	Induction of temperate bacteriophage $\lambda$ Survival of bacteria	Threefold increase ( $p < 0.010$ ) 0	S.V Komarov M.P. Bragin
<i>Tetrahymena</i>	Cellular proliferation Cell size Cell shape DNA content Protein content	Accelerated ( $p < 0.05$ ) 0 More spherical 0 Decreased ( $p < 0.05$ )	M.G. Tairbekov I.B. Raykov
<i>Chlorella</i> (auto-trophic culture)	Number of autospores Growth in biomass	Increase 0	G. I. Meleshko
<i>Wolffia</i>	Growth Aging	Stimulation Acceleration	V.M. Abramova
<i>Haplopappus</i> (tissue culture)	Lipid peroxidation Cell ultrastructure	Increase 0	Ye.L Kordyum
Oocytes: <i>drosophila</i> guppies	Ploidy of nuclei Development of new generation	0 0	A.A. Neyfakh
tritons	Size of oocytes Nucleoli number, size	Increase Increase	L.B. Belousov N.L. Delone
Female <i>Drosophila</i>	Frequency of meiotic crossing over	More or less as a function of locus	A.V. Smirnova
Stick insect eggs	Embryonal development Hatching of larvae	0 Increased death, anomalies	Yu.A. Zakhvatkin Kh. Byuker
Guppies	Embryonal development Vestibular apparatus Swim bladder	0 0 Not filled with air	L. R. Pal'mbakh
Darkling beetles	Period of spontaneous circadian rhythms	Shortened ( $p < 0.005$ )	A.M. Alpatov V.B. Chernyshev
Impatiens (shoots)	Root cap regeneration	0	V.G. Chuchkin V.B. Ivanov
Planaria	Body regeneration	0	A.M.. Morozov
Tritons	Regeneration of limbs crystalline lens	Inflight — 0; 2 weeks postflight — acceleration	V.I. Mitashov
Primate lympho-cytes	Sister chromatid exchanges Number of nucleoli	Non-significant increase Increase	N.L. Delone S.M. Kuzin

## SPACE BIOLOGY AND MEDICINE

P1177(26/90) Grigor'yev AI, Morukov BV.

### ***370-Day antiorthostatic hypokinesia: Goals and research protocol***

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 47-50; 1989.

[9 references; none in English]

Space Biology and Medicine; Cardiovascular and Respiratory Systems; Cardiovascular Deconditioning; Body Fluids; Musculoskeletal System; Metabolism; Gastrointestinal System; Hematology; Immunology

Humans, Males

Hypokinesia with Head-Down Tilt, Long-Term; Prophylactic Countermeasures, Physical Exercise; Drugs; LBNP; Karkas Suit; Adaptation

**Abstract:** Long-term manned space flights are not possible without the use of prophylactic countermeasures to protect cosmonauts against the adverse physiological effects of weightlessness, and to support a high level of cosmonaut performance and successful readaptation to postflight conditions on the ground. The current system of prophylactic countermeasures has enabled humans to remain in space under conditions of weightlessness for up to 326 days.

However, the implementation of long-term manned space flights has confronted space medicine with a series of new problems, the solution of which will determine whether it is possible to further prolong space flights.

Under prolonged exposure to microgravity changes in the musculoskeletal system, metabolism, cardiovascular, digestive, and urinary functions, the red blood system, and immunological response increase in significance. If these shifts are to be prevented, it is not enough to use prophylactic countermeasures that mainly target cardiovascular functioning. The use of specific countermeasures for prophylaxis and correction is required. Adaptation of the cardiovascular system to conditions of microgravity is also not limited to the acute period; as space flight duration increases, the problems of organ hemodynamics, microcirculation, and lymph production, which are closely linked to regulatory shifts, and changes in organs at the tissue and cellular levels, take on primary importance.

The system designed to prevent the adverse effects of space flight must be more flexible, complex, and capable of preventing as well as correcting the changes that occur.

The most widely accepted ground-based model of weightlessness that can be used for a prolonged period involves subjecting humans to strict bedrest with head-down tilt. Using this paradigm, researchers, physicians, and developers of prophylactic countermeasures can work collaboratively to monitor, adjust, individualize, and supplement the use of countermeasures and also to validate the efficacy of various prophylactic systems.

The objective of the current research, involving a 370-day period of hypokinesia with head-down tilt, was to optimize the set of prophylactic countermeasures intended for use on long-term space flights.

The first and one of the most important goal was to optimize the physical exercise (conditioning) system, including: investigation of the efficacy of exercise of different parts (of the body); evaluation of the extent of deconditioning after breaks in exercise at various intervals of bedrest; development and validation of various schedules for recovery of physiological functioning after a long interval of lack of physical exercise under conditions of

## SPACE BIOLOGY AND MEDICINE

bedrest; validation of exercise equipment proposed for future use and of devices that automatically control physical exercise and concurrent medical monitoring.

A second objective was to study the efficacy of drugs in preventing metabolic shifts in muscle and bone tissue, metabolism, and providing appropriate levels of anabolic and catabolic processes during periods of intense physical exertion.

The third objective involved evaluation of the efficacy of measures to correct hemodynamic shifts and fluid-electrolyte homeostasis.

Subjects in the research were 10 apparently healthy male volunteers, aged 27-42, who were divided into 2 groups containing 5 subjects each. Subjects in the first group utilized a set of prophylactic countermeasures, including physical exercise, as well as drugs to correct metabolism, status of bone tissue, and digestive function throughout the entire period of bedrest.

For both groups the exercise regimen followed a 4-day microcycle (3 days of exercise and 1 day of rest). Exercise was performed in a horizontal position on the "Podveska" treadmill device and on a bicycle ergometer hooked up to the "Fiziotest" instrument, which controlled the exercise schedule in accordance with a predetermined program, as well as on the basis of feedback from pulse rate. In addition, the program included a set of exercises with expanders.

During the baseline period and twice during bedrest, group 1 subjects underwent ultraviolet irradiation with the goal of enhancing nonspecific resistance and countering insufficient formation of Vitamin D.

Group 2 subjects spent 120 days under conditions of hypokinesia with head-down tilt without utilization of any sort of prophylactic countermeasures; during the subsequent 2 months, physical conditioning exercises were used to facilitate recovery of functional capacity under conditions of bedrest. Starting on day 180 of bedrest, this group was used to validate proposed future programs of physical exercise and auxiliary methods for increasing the efficacy of physical conditioning exercises and facilitating recovery after exercise. Group 2 subjects were given corrective drugs, as indicated, after 150 days of bedrest.

During the final stage of the experiment both groups were given the most effective exercise regimen and corrective measures for fluid-electrolyte metabolism and hemodynamics. For this purpose the "Karkas" anti-g suit (which does not use a bladder) was worn and salt-water and multivitamin-protein supplements were administered.

To increase orthostatic tolerance, lower body negative pressure combined with low levels of electrical muscle stimulation was used with the second group. The general objective of research protocol, which is presented in the table below was to evaluate the efficacy of the prophylactic countermeasures at the different stages of treatment.

Once every 2 months, at the end of each physical exercise regimen, a set of physiological studies was performed, including a tilt test, a maximal exercise test on the treadmill, noninvasive study of bone tissue, study of the status of the muscular system and evaluation of level of physical fitness, biopsy of calf muscles, biochemical studies of blood and urine, lower body negative pressure tests, etc.

On days 120, 240, and 360 of bedrest, acceleration tolerance was tested on a centrifuge. An in-depth examination of cardiovascular function, and hematological studies were performed every month throughout the bedrest period. Mineral balance was studied during the baseline period and throughout bedrest, a biopsy of the iliac crest was performed at the beginning and termination, of bedrest and, in the case of group 2, on day 115 of treatment.

## SPACE BIOLOGY AND MEDICINE

Preliminary results attest to the efficacy of the set of countermeasures used during the 370-day period of bedrest.

Table: Research Protocol

<b>Cardiovascular and Respiratory System</b>	
<b>At rest</b>	<b>Provocative tests</b>
1. EKG, polycardiography, impedance plethysmography	1. Endurance of +G <sub>x</sub> acceleration
2. Dynamic EKG	2. Postural tests
3. Ultrasound studies of the heart and vasculature	2.1 Tilt test in upright position with radioisotope studies
4. Radioisotope studies: blood redistribution: regional and organ hemodynamics tissue and regional lymph flow perfusion of the visceral organs	2.2 Head-down tilt test (using ultrasound-tests)
5. Oxygen conditions in tissue and regional blood flow studied through polarography	3. Exercise tests
6. Biomechanics of respiration and measurement of reserve capacity of diaphragm	3.1 Test of maximal physical exercise on the treadmill
	3.2 Exercise test on bicycle ergometer with ultrasound tests with radioisotope tests using "Fiziotest" device
	3.3 Exercise test on treadmill in supine position
<b>Musculoskeletal System</b>	
<b>Bone tissue status</b>	<b>Muscle system and neuromuscular apparatus</b>
1. Noninvasive measures	1. Speed/strength properties and muscle work capacity
1.1 Monophoton absorptiometry (heel bone, calf, forearm)	1.1 Isokinetic dynamometry (evoked contraction)
1.2 Biphoton absorptiometry (spine, neck, and femoral diaphysis)	1.2 Isometric testing of muscle groups
1.3 Computer tomography (spine, femur, calf)	1.3 Athletic testing of muscle groups
1.4 Neutron-activated analysis of calcium levels (foot, spine, hand)	2. Anthropometry
1.5 Ultrasound diagnosis	3. Reflexometry (T- and H-reflexes)
2. Biopsy of the iliac crest (physical chemical properties, mineral composition, strength)	4. Motor regulation (regulation of posture, fine motor movements, activity of motor units, integrated tremography)
	5. Study of biopsied muscle tissue (morphological and histochemical studies.)



# SPACE BIOLOGY AND MEDICINE

## Metabolism and Its Regulation

### Biochemical Studies

1. Balance studies
2. Biochemical studies of blood and urine
  - 2.1 Blood ions
  - 2.2 Protein levels, protein fractions of blood, products of nitrogen metabolism in blood and urine
  - 2.3 Lipid spectrum of blood
  - 2.4 Lipid peroxidation
  - 2.5 Carbohydrate metabolites
  - 2.6 Blood enzymes
  - 2.7 Base levels of hormones and biologically active substances in blood, their renal excretion
3. Diurnal rhythms of parameters of fluid-electrolyte metabolism and its regulation system

### Provocative Tests

1. Calcium gluconate test (administered orally or intravenously)
2. Insulin test
3. Glucose loading test (including study of hormonal parameters)
4. ADH test
5. Study of biochemical parameters in response to exercise test
6. Study of biochemical parameters when measures to correct fluid-electrolyte metabolism are used
7. Study of biochemical parameters in response to vestibular stimulation

## Digestive System

1. Investigation of digestive enzymes in blood, feces, and intestinal juice
2. Investigation of acid-forming functions of the stomach (acid test, intragastric pH measurement)
3. Duodenal probing and study of the stomach acid spectrum
4. Ultrasound studies of the digestive organs

### Hematological Studies

1. Study of peripheral blood
2. Study of hemoglobin mass
3. Study of iron metabolism
  - 3.1 Ferrocyrro?? loading
  - 3.2 Radioisotope method
4. Study of erythrocyte metabolism

### Immunological Studies

1. Factors of cellular immunity
2. Factors of humoral immunity
3. Immunological mechanisms for regulating calcium metabolism and bone tissue status

## SPACE BIOLOGY AND MEDICINE

CR12(26/90)\* Drozd YuV.

**Report on: Twenty-first Symposium on Space Biology and Medicine** (Baranov-Sandomerski, June 1988)

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(5): 93-96; 1989.

**Key Words:** Space Biology and Medicine; Human Performance; Radiobiology; Equipment and Instrumentation; Operational Medicine; Musculoskeletal System; Weightlessness; Acceleration; Prophylactic Countermeasures; Hypodynamia; Hypokinesia; Psychology, Stress; Space Flight; COSMOS-1887; Nutrition; Metabolism; Life Support Systems, CELSS; Neurophysiology, Motion Sickness; Sleep; Immunology

From June 6-10 1988, a symposium was held by the Intercosmos Working Group of Socialist Nations on the topic of space biology and medicine in the city of Baranov-Sandomerski (Poland). Sessions were devoted to the following topics: experiments on biosatellites, possibility of maintaining human performance, human and animal physiology in extreme conditions, biological methods for evaluating radiation injuries, design and production of apparatus for solving problems of space biology and medicine.

At the plenary session a paper was presented entitled, "On the goals and objectives of the planned space medical laboratory MEDILAB" (A.I. Grigor'yev, Ye.A. Il'yin, S.F. Kholin et al., USSR). The research program planned for this project will enable diagnosis and treatment of disease under conditions of space flight, prevention and correction of the physiological effects of space flight factors, monitoring and management of the environment, control of vital processes during space flight, identification of the body's reserve capacities, and determination of characteristics of interaction in a man-machine system as applied to space flight conditions.

**Weightlessness.** Many papers were devoted to one of the most urgent problems in space biology and medicine -- the physiological effects of weightlessness. Planned biosatellite experiments will focus on further study of the mechanisms underlying the effects of weightlessness on interactions of the sensorimotor system, systemic and regional circulation, the musculoskeletal system, metabolism, biological rhythms, tissue and organ regeneration, and growth and development (Ye.A. Il'yin, V.I. Korolkov, V.K. Golov, USSR). Biosatellite experiments have demonstrated a decrease in the diameter of muscle fibers in the hearts of rats after space flight (V. Baran'ska, Poland). During early stages of simulated weightlessness, changes in motor fibers are associated with effects of reflex hypotony, and during later stages with relatively inert trophic adaptive shifts (L.S. Grigoryeva, USSR). A number of works have demonstrated the effects of weightlessness on the functions of a variety of organs and systems: changes in the mucous membranes of the stomach in animals (A. Pozhgay, Ya. Khiddeg, Ye. Tot, Hungary); decrease in the maximal relative deformation and increase in the modulus of elasticity in bones during the first 7 days of simulated weightlessness followed by decrease in modulus of elasticity as osteoporosis develops (A.V. Bakulin, V.Ye. Novikov, USSR); increased concentration of ATP and Krebs cycle enzymes, i.e. activation of metabolic processes serving to increase the functional capacity of cells (A.S. Ushakov, USSR; S.S. Brantova, Czechoslovakia). Weightlessness has been found to decrease the vital capacity of the lungs while the Tiffeneau index (ratio of forced expiratory volume to vital capacity; ventilation index) remains unchanged, and peak inspiratory flow rate decreases (A.M. Genin, V.M. Baranov et al., USSR). Individual differences were noted in weightlessness in two monkeys with regard to blood filling in the pulmonary circulatory tract and cerebral hemodynamics. In one, cardiac output increased, external respiration decreased, fluid volume in the chest cage increased, and weight loss occurred. In the other monkey cardiac output decreased while external respiration, fluid volume in the chest cage, and body weight all increased.

## SPACE BIOLOGY AND MEDICINE

Experience with multimonth space flights has shown that the effects of long-term exposure to weightlessness may be effectively controlled with a set of prophylactic countermeasures (O.G. Gazonko, Ye.B. Shulzhenko, A.I. Grigoryev et al., USSR).

**Acceleration.** The physiological effects of acceleration remain a pressing problem of aerospace medicine. Measurement of blood pressure using the technique developed by Ya. Penyaz (involving the Czechoslovak "Servotonometr" instrument) is a promising method for predicting cardiovascular functioning in response to acceleration (A.R. Kotovskaya, I.F. Vil'-Vil'yams, USSR; Ya. Penyaz, Czechoslovakia). An analogous Soviet instrument has been developed (S.S. Rvachev, V.M. Shchebakov). Noteworthy data indicate that exposure to pulsed acceleration of +5g with 2-3 minute breaks leads to greater decreases in glycogen in the liver and a greater need for oxygen than comparable uninterrupted acceleration (V. Kovalski, S. Vrublevski, Ya. Pozhinski, Poland). Special training procedures increase acceleration tolerance in individuals with initial low tolerance (S. Baranski et al., Poland).

**Hypodynamia, hypokinesia.** Due to limitations on the size of current spacecraft and space stations, hypodynamia and hypokinesia continue to be pressing problems. Deconditioning, occurring in response to long-term hypokinesia under laboratory conditions, substantially alters energy supply in graded physical exercise. Under these conditions, there are decreases in blood glucose, triglycerides, nonesterified fatty acids, and activity of Krebs cycle enzymes (I.A. Popova, Ye.A. Nosova, V.M. Mikhaylov, USSR). When monkeys were subjected to a 14-day period of hypokinesia with head-down tilt, they displayed depression in activity of  $\beta$ -cells in the Langerhans' islands of the pancreas and a compensatory increase in secretion of insulin-like protein by the salivary glands. (Ye.A. Savina, A.S. Kaplanskiy, G.N. Durnova et al., USSR). Rats exposed to hypokinesia developed thrombocytopenia and accelerated coagulation and fibrinolysis of blood during weeks 1-2 of a laboratory study, with a subsequent tendency for these effects to normalize by week 3, in association with changes in secretion of corticosterone and other hormones (P. Groza, Ye. Nicolesceau, Romania). Rats exposed to space on COSMOS-1887 displayed weight loss in the thymus, spleen, myocardium and testes, and a weight gain in the liver, kidneys, and adrenal gland (Ye.A. Il'yin, Ye.A. Savina, USSR; S. Baranski, Poland). Other authors also noted acceleration of lipolysis, increase in lipomobilization, hyperglycemia and moderate fatty dystrophy of the liver combined with accumulation of glycogen (Ye Akersova, Czechoslovakia; I.A. Popova, USSR).

**Stress.** Interesting facts were presented indicating that psychoemotional stress is associated with decreased blood pH (Ya. Sykora, Z. Dragota, Czechoslovakia) and that strong negative emotions induce clear interhemispheric asymmetry of the thermal fields of the brain (G.D. Kuznetsova, G.G. Shlyk, A.N. Ivanov, et al., USSR). The greatest tolerance of stress was found in athletes with low levels of reactivity (A. Zmudski, Ya. Terelyak, Poland). Administration of substance P (neuropeptide) intranasally in a dose of 5  $\mu$ g/kg per day to some extent normalizes thought processes, improves perception, and fosters normalization of psychomotor and autonomic reactions in subjects under stress (K. Hecht, GDR).

**Nutrition in space. Metabolism.** Disruption of protein synthesis occurs under exposure to space flight. There is a decrease in concentration of nucleic acids in the spleen, thymus, and liver without signs of decay of deoxyribonucleotides (Ye. Mishurova, Czechoslovakia; I.A. Popova, USSR). Polyamines stimulate protein synthesis at the level of RNA transcription, while level of putrescine may serve as an indicator of the biosynthesis of protein in the brain structures during space flight (V.Yu. Kovalev, USSR). A balanced and rational diet in space, including sources of nutrition that can reproduce themselves in a closed ecosystem, is of particular importance here.

The water fern *Azolla pinnata* is distinguished by its high level of protein (20% of dry mass) with a good amino acid composition and a significant quantity of lipids (14%) and may be used in

## SPACE BIOLOGY AND MEDICINE

CELSS (A.A. Antonyan, G.I. Meleshko, USSR; Hguen Kh. Tkhyuk, Viet-Nam). The quail is an efficient component of an ecosystem from the standpoint of meat and egg production (V.F. Mishchenko, Ye.A. Shepelev, USSR; R. Bodya, Czechoslovakia). Ingestion of 30-40 g of the yeast *Kluvermices fragilis* daily does not cause metabolic disturbances, and is associated with only an insignificant increase in concentration of nonprotein nitrogen and uric acid in blood and urine (A. Viamendez, Kh. Ilnait, Cuba). A protein-vitamin supplement developed by specialists from Poland facilitates better adaptation to exercise (G. Malevich, S. Baranski, Poland; M.S. Belakovskiy, USSR).

Soviet and Czechoslovak specialists have developed the "Plazma-02" instrument for biochemical investigations of trace quantities of biomaterial. This instrument may be used for the study of the metabolic status of humans under extreme conditions (I.A. Popova, Ye.G. Vetrova, V.B. Noskov, USSR).

**Motion Sickness.** Level of vestibular tolerance is an important factor in the selection and training of cosmonauts and pilots. The nystagmic reaction to rotational and rotation-swinging stimulation will be used to estimate the fitness of flight crews (I. Birke, GDR). The most accurate estimate of the efficacy of pharmacological agents in preventing motion sickness is produced by use of the slow-rotating room. (R.R. Galle, G.A. Susakova, USSR; G. Bodo, Hungary).

Transmission of a descending galvanic current through both labyrinths of individuals with low levels of vestibular tolerance increases resistance to experimental induction of motion sickness in 70% of the cases (L.N. Kornilova, O.N. Klyushnikova, USSR; P. Duda, Czechoslovakia). Adaptive biofeedback is a promising method for curtailing motion sickness (S.A. Smirnov, I.B. Kozlovskaya, G.S. Ayzikov, USSR). In experiments on animals it was demonstrated that intracerebroventricular administration of substance P, hydro-undecapeptide, and certain endorphins to animals have vestibuloprotective (i.e., antinauseant) effects (Yu.V. Drozd, USSR). Hungarian specialists have proposed the use of Yumex (selegiline hydrochloride quinine), which relieves symptoms of motion sickness without impairing operator performance (G. Bodo, K. Elkan, G. Bentse).

**Psychoemotional Issues. Sleep.** One of the most important aspects of space medicine is the study of psychoemotional issues (V.I. Myasnikov, USSR). Sleep is an informative criterion for assessing adaptive behavior in humans exposed to extreme conditions. An important cause of sleep disturbance in cosmonauts is desynchronization of the circadian system (B.S. Alyarkinskiy, USSR). An apparatus has been developed that makes it possible to automatically determine stage of sleep by means of a wave analysis (M. Daskalova, V. Kolev, Czechoslovakia). Adaptation of monkeys to space flight is achieved through restructuring of the REM sleep system (G.G. Shlyk, V.S. Rotenberg, USSR). The Korteks-2 unit developed by specialists from the USSR and Cuba (M. Estevez, I. Fernandez, Cuba; V.I. Myasnikov, USSR) makes it possible to conduct various psychophysiological tests. The methods of evoked potentials and spectral analysis of EEG are effective in the diagnosis of disorders in the sensory system in anticipation situations and may be used for occupational selection (O.I. Shevchenko, USSR). Activation of lipid peroxidation serves as one of the manifestations of neuroemotional stress. A correlation has been found between levels of products of lipid peroxidation in saliva and reliability of operator performance (V.M. Puko, V.I. Gushchin, USSR). It has been found that physical exercise has a favorable effect on psychological performance of operators under conditions of long-term hypokinesia (I.P. Ponomareva, O.P. Zhidkova, USSR; Ya. Khideg, Hungary). A report by P. Remesh and Ya. Khideg (Hungary) concluded that individuals with diminished tolerance of hypoxia may display sharp decreases in information processing capacity, even when their general state appears to be good.

**Immunology.** Research has shown that simulation of the effects of space flight factors (particularly through hypokinesia) leads to dysbiotic changes in intestinal microflora,

## SPACE BIOLOGY AND MEDICINE

depression of bifidobacteria and bacterioids, and increased levels of opportunistic flora. The activity of peptidases is inversely correlated with quantity of bacterioids and yeast; activity of invertase is inversely correlated with concentration of staphylococci and proteus, i.e., there is a close relationship between enzymes and intestinal microflora (K.V. Smirnov, N.P. Liz'ko, R.A. Pechenkina, et al., USSR). Space flight is associated with a moderate decrease in the quantitative and functional characteristics of normal killers, a decrease in the proliferative activity of T-lymphocytes, development of delayed hypersensitivity to opportunistic microflora, and also a tendency for activity of T-suppressors to increase, and a decrease in OKT4+ Hiltner?? cells (I.V. Konstantinova, Ye.F. Vasilyeva, et al, USSR).

**Biological methods for assessing radiation damage.** A number of papers were devoted to the development of new radioprotectors. The presence of marked changes in electrophysical parameters (equivalent resistance, equivalent electromotive force) at certain points on the skin suggests the possibility that such indicators can be used as the basis for developing a method for biological tracing of irradiation (T.Ya. Ryabova, V.B. Silin, USSR; V. Yakoubek, Czechoslovakia). Adenosine-5-monophosphate (AMP) has an antiradiation effect in mice, comparable to the efficacy of other preparations of the adenyl series (V.N. Andrushchenko, K.S. Chertkov, USSR). Data were obtained concerning the decrease in the genetic effects of ionizing radiation with prophylactic administration of the drug WR-2721 (A. Bayrakova, Bulgaria). The immunodilator sodium diethyldithiocarbamate facilitates postradiation restoration of the hemopoietic tissues of mice (M. Goshek, Ya. Shikulova, Czechoslovakia). Betamide also had a beneficial effect on postradiation recovery of hemopoiesis and, moreover, decreased the amount of chromosome damage in bone marrow (T.P. Pantev, S. TS. Topalova, Bulgaria; Z.M. Mosina, USSR). The radioprotectant effects of AMP are enhanced when magnesium asparaginate is used simultaneously (M. Pospishil, M. Ya. Netikova, A. Kozybik, Czechoslovakia). A lyophilized water extract of the biomass of *Chlorella reisseri* (ivastimul) algae has a beneficial effect on recovery of hemopoiesis after  $\gamma$ -irradiation (D. Rotovska, Czechoslovakia). A good protective effect was noted for adeturon after irradiation by corpuscular particles (V. Genchova, Ts. Marinov, T. Pantev, Bulgaria). Experiments on mice have demonstrated that riboxin has a strong antiradiation effect (K.S. Chertkov, USSR; M. Pospishil, Czechoslovakia).

## SPACE BIOLOGY AND MEDICINE

P1194 (26/90)Kovalenko YeA, Kasyan II

### *On the Pathogenesis of Weightlessness*

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Space Biology and Medicine; Neurophysiology, Space Motion Sickness; Body Fluids;  
Cardiovascular and Respiratory Systems; Endocrinology; Musculoskeletal System;  
Enzymology; Metabolism, Bioenergetics

Humans, Cosmonauts, Rats

Weightlessness, Pathogenesis; Deconditioning; Adaptation; Space Flight, Long-Term; Salyut,  
Soyuz, Weightlessness Simulations, COSMOS; Prophylactic Countermeasures; Physical  
Exercise, LBNP

**Abstract:** Soviet data have demonstrated that humans may live and work in space for an entire year without severe physiological changes, provided an extensive program of prophylactic countermeasures is adhered to. Since weightlessness is a factor to which humans have not previously been exposed, and since there is currently no precise data concerning immediate or remote effects of long-term exposure, the authors consider it of benefit to analyze the effects of weightlessness from the standpoint of classical pathophysiology. In classical pathophysiology, one starts by accurately determining the nature of the etiological factor and describing its physical, chemical, and biological effects. Next, one defines the conditions under which it operates, since they may attenuate or enhance the effects of the etiological factor itself. Finally, one must identify the major pathogenic components in the development of the physiological change or disorder and trace the course of the entire series of changes. In addition, it is essential to identify the protective or compensatory shifts in the physiological systems affected. These shifts must be considered not merely as adaptive responses, as is typically done in analyzing the effects of weightlessness, but as protective responses to a deviation from the norm. The authors consider this approach to analysis of the effects of weightlessness novel, theoretically significant, and timely, since space flights are becoming extremely long in duration. It is well known that pathological changes may result if exposure to virtually any factor markedly increases, or even decreases, in intensity or duration.

In their discussion the authors consider weightlessness primarily as a potential cause of certain clearly observable deviations from the norm. They assume that these changes occur under conditions of weightlessness, even after the adaptation period is complete, and may intensify as duration of exposure increases. It follows from this hypothesis that when potent countermeasures are not utilized, weightlessness may continue to induce pathological changes.

The practical results of the Soviet use of countermeasures during long-term space flights (up to 237-326 days) attest to their efficacy in eliminating the major components of the pathogenic effects of weightlessness. During space flight humans are exposed not only to weightlessness, but to a systematic and constantly improving program of prophylactic countermeasures. Consequently, it is not possible to speak of the unadulterated effects of weightlessness. We are not simply seeing the effects of a potentially pathogenic factor, but are observing them under conditions that significantly attenuate these effects. Thus, the continued observation of changes in functioning or biochemical parameters observed in weightlessness and the rather severe changes in a number of parameters that persist for some time postflight attest to the inadequacy of the countermeasures. Painsstaking study of these changes, even those that are not always clearly manifest, is of great theoretical significance for the understanding of the overall pattern of the possible mechanism underlying the effects weightlessness. Such studies are of practical importance as well, since they pinpoint what adverse changes, in what systems, and at what level cannot yet be averted through use of prophylactic countermeasures during prolonged exposure to weightlessness.

## SPACE BIOLOGY AND MEDICINE

What are the pathogenic components of the physiological effects of weightlessness? The first important change occurring under conditions of weightlessness is the elimination of deformation (i.e., compression) of tissues, organs, and systems due to the force of gravity. The afferent signals from tissue and organ receptors that heretofore had been deformed and distended are, to a significant degree, eliminated, attenuated, or altered. This is the first neurogenic mechanism underlying one of the major pathogenic components of weightlessness effects -- the elimination of deformation. The next important pathogenic component of weightlessness effects is the elimination of the hydrostatic blood pressure gradient and the redistribution of body fluids, most significantly blood, to the upper body, due to elimination of their natural weight. This leads to some distension of the vessels and tissues containing blood and other fluids. These two major components of weightlessness effects may in turn lead to a whole series of derived pathogenic phenomena (see Figure).

Under conditions of weightlessness, changes occur in the nature of afferent stimulation from the receptors of a number of systems and organs: the otoliths, tactile receptors, proprioceptors, and interoceptors of organs and tissues that on Earth normally undergo deformation and mechanical stress, as well as the vascular areas, hollow organs, etc. Due to the displacement of blood into the upper body, the strength of impulses from the vasculature of the lower body decreases while that from the upper body vasculature increases substantially. The pattern of afferent stimulation is altered. This effect of weightlessness is, as a rule, experienced by all cosmonauts. Thus, for example, the first crew on the Salyut-6 space station experienced an unpleasant sensation of the rushing of blood to the head as early as hours 3-4 of exposure to weightlessness. All crewmembers of the third Salyut-7 crew experienced the sensation of rushing of blood to the head during the first 2 days of flight, after which the sensation passed and did not interfere with performance of the flight program.

During long-term flights, there is a pronounced displacement in body fluids which, as a rule, has led to an upward shift of the cosmonaut's center of gravity. For example, leg volume decreased by an average of 13% compared to baseline in American astronauts on Skylab. Analogous changes were noted in Soviet cosmonauts during long-term flight. Thus, on a 140-day flight, calf volume in both cosmonauts decreased by 11-13% after 10 days, and by 80-100 days had decreased by 20-30%. This indicates that a substantial displacement of body fluids is followed by a decrease in the mass of the calves and legs. Other pathogenic phenomena ensue, triggered primarily by the redistribution of blood and other body fluids to the upper body (cf. Figure). Displacement of blood into the upper body leads to increased stimulation from the carotid sinus and aortal reflexogenic zones, i.e., depressor reflex activity is intensified.

Excess filling of the ostia of the venae cavae enhances the Bainbridge reflex. In addition, all the receptor fields of the meninx and vascular regions of the head and tissues, which are filled with extra blood, lymph, and interstitial fluid, trigger a number of mechanisms that serve to eliminate excess fluid from the head and upper body.

At the same time, blood filling of the vasculature of the pulmonary circulatory tract increases and pressure in the cardiac auricles rises. These phenomena may trigger the next important group of effects of weightlessness: changes in regulation of fluid-electrolyte metabolism. The major mechanism through which this effect is realized involves stimulation of the receptor zones of the auricles, sending signals to the supraoptic nucleus of the hypothalamus, which in turn induces decreased secretion of antidiuretic hormone and attenuates the Henry-Gauer reflex, leading to increased diuresis. However, this explanation of the mechanism underlying the connection between circulation and fluid-electrolyte metabolism in weightlessness is patently incomplete, although it has been offered repeatedly in recent literature.

Recently, a major discovery on the endocrine function of the heart has radically altered our ideas concerning regulation of hemodynamics, as well as of fluid-electrolyte metabolism. It has been established that the cardiac auricle synthesizes and secretes into the blood a peptide hormone -- the so-called atrionatriuretic factor (ANF). This hormone has a variety of effects, but in particular regulates vascular tonus. The auricular hormone attenuates vascular tonus in the presence of angiotensin II and noradrenalin, even when their concentration exceeds that of ANF by an order of magnitude. The heart thus has the capacity to alter the chemical signals sent by the cells of other regulatory organs. It has been demonstrated that, after its release into the blood, the effects of ANF develop rapidly and attain a maximum after 1-2 minutes. Diuresis and excretion of  $\text{Na}^+$  and  $\text{Ca}^{2+}$  increase by a factor of 10, but secretion of  $\text{K}^+$  ions increases only slightly. In other words, when the baroreceptors of the auricle are stimulated mechanically, increased secretion of ANF induces profuse excretion of urine and electrolytes, and this leads to a marked decrease in circulating fluid volume. This then is a new and highly important component in regulation of fluid-electrolyte metabolism and changes in circulating blood volume and vascular tonus, one that lowers blood pressure and alters hemodynamics.

It is to be expected that weightlessness, which causes blood redistribution and a substantial increase in blood filling of the auricle, would lead to increased ANF secretion. This is a likely area in which to look for changes in regulation of fluid-electrolyte metabolism and circulation that have been influenced by the endocrine function of the auricle. Work by C. Leach has demonstrated that under conditions of weightlessness, when venous pressure is elevated and the receptors of the auricle are stimulated, ANF secretion intensifies, increasing renal excretion of fluid and electrolytes, which, in turn, leads to a change in circulating blood volume. However, this is accompanied not by a decrease, but by an increase in the level of antidiuretic hormone. For this reason, the role and significance of ANF as an important component in regulation of fluid-electrolyte metabolism and circulation has already begun to be considered in the analysis of space flight results. However, this issue requires greater attention and more detailed investigation.

Another important component in the pathogenesis of weightlessness is unloading of the antigravity muscles. The primary relevant factor here is the overall decrease in muscle tonus due to elimination of the need to overcome the force of gravity when moving. Attenuation of muscle tonus and the sharp decrease in muscle function are two of the most important components of the entire pathogenic process, since they lead to decreased catabolic and anabolic support of muscle function. It is also not surprising that the first manifestation of deconditioning to be observed affects the regulatory processes of the motor system. The well-developed coordination of complex motor regulation begins to fail.

Other extremely important components of the pathogenesis of weightlessness are the elimination of skeletal loading, alteration of bone structure and metabolism (disruption of protein, phosphorus, and calcium metabolism), and bone decalcification (demineralization). After flights 3 days in duration on Soyuz-4 and -5, bone demineralization was not significant; however, when flight duration increased to 18 days on Soyuz-9, decalcification of the heel bone increased on the average by a factor of two and in the bone of the hand by almost a factor of three. Further increase in the flight duration to 24 days on Soyuz-11 led to a sharp decrease in the optical density of an x-ray of bone tissue. In the postflight period this decrease averaged 16%, ranging from 13.7 to 18% compared to baseline.

Simulation of weightlessness through long-term hypokinesia revealed that after 20, 70 and 100 days of hypokinesia, optical density of the heel bone decreased by 8.5, 11.6 and 26%, respectively. A number of studies on animals revealed inhibition of bone neoformation, development of osteoporosis, and demineralization of bone tissue, even after flights as short as 18.5 to 22 days. The development of osteoporosis and decrease in density of bone mineralization



## SPACE BIOLOGY AND MEDICINE

led to a decrease in bone strength, resulting in fractures in some animals in response to the impact of biosatellite landing. Postflight decrease in bone density has been established in animals other than rats. The finding of increased numbers of protein-calcium urinary casts in the renal tubules of rats flown on COSMOS-782, -936, and -1129, evidently associated with bone demineralization and increased excretion of calcium, is also extremely serious. Evidently this component of the pathogenesis of weightlessness can also lead to serious changes in a number of other physiological systems. In this light, changes in calcium homeostasis are worthy of particular attention. According to current ideas, a great number of functions are performed by calcium and calmodulin in the body. However, as yet no data exist on changes in calmodulin in response to weightlessness.

One of the important characteristics of physiological functioning can be observed through data concerning changes in external respiration in response to weightlessness. It is natural that under conditions of weightlessness, when blood filling of the pulmonary circulation tract and rate of venous return increase, the rate at which venous blood enters the lungs also increases. There is some increase in blood pressure in the vessels of the pulmonary tract, especially those in the lungs. As a result, the ratio between blood perfusion rate and pulmonary ventilation, which is well regulated under conditions of normal gravity, alters. At the same time, due to changes in the normal topography of perfusion in the pulmonary tract, a tendency may arise for some increase in pulmonary ventilation in order to maintain the oxygenation of the greater volume of venous blood entering pulmonary vessels. As yet only a small amount of actual data are relevant here. Thus on Skylab, an increase in resting pulmonary ventilation was noted in seven out of nine astronauts. In one of the remaining astronauts, inflight pulmonary ventilation remained at its preflight value, while in the other pulmonary ventilation decreased with respect to preflight data. In the commander of another space station flight, inflight pulmonary ventilation increased from 7.5 to 9.98 l/min, while in the pilot this value increased from 6.69 to 8.47 l/min.

During the flight of the visiting crew to the Salyut-6 orbital station, an experiment revealed an 18-34% increase in resting respiratory minute volume (RMV) compared to preflight data in the commander and the flight engineer. Genin and co-workers attribute this to an increase in respiration rate over baseline parameters. During 140- and 175-day flights, RMV changed in different directions in different cosmonauts. At the beginning of the flight, both the commander and the flight engineer (on day 10 of the 140-day flight and day 20 of the 175-day flight) displayed a decrease in RMV compared to values recorded preflight. By day 110 of the 140-day flight, RMV had stabilized in both crewmembers and had virtually attained its preflight value, while in the commander of the third prime Salyut-6 crew, minute volume increased from 4 to 10 l/min beginning on day 50 and continuing to the end of the 175-day flight.

Thus, the existing data suggest that external respiration most frequently displays a tendency to intensify under conditions of weightlessness. However, the reason for this change and the mechanism through which it occurs clearly have not been studied in sufficient detail. It may be assumed that, as was noted above, the increase in perfusion of the vessels of the pulmonary tract leads to an increase in pressure and causes the alteration of the normal (terrestrial) value of the ratio of perfusion to ventilation in the lungs that is observed under exposure to weightlessness, especially during the initial period. In addition, it may be postulated that, despite the absence of constant exposure to the force of gravity, the unaccustomed and often elevated amount of effort needed to maintain a position and perform ordinary motor acts before new coordination skills have been fully developed, as well as the occurrence of additional vestibular stimulation and some degree of situational stress during initial exposure to space, are conducive to increased external ventilation and gas metabolism. This situation may lead to changes in the degree of oxygenation of blood in the lungs, and also to some degree of change in the vascular beds of tissues, especially in the upper body, possibly accompanied by regional engorgement. Extremely interesting data were obtained after exposure of rats to weightlessness

## SPACE BIOLOGY AND MEDICINE

for a 22-day period. The number of functioning capillaries in the muscles of their hind legs decreased by 30%, attesting to a decrease in vascularization of this tissue. All this leads to a decrease in oxygenation both in blood and tissue in the affected part of the body. Evidently there may be a general decrease in blood oxygenation in the lungs, as well as in regional tissue oxygenation. To further investigate this possibility, a special experiment was performed to study the dynamics of oxygen tension in the lungs. It was established that during flight, oxygen tension decreased in tissues of cosmonauts from  $56 \pm 2.0$  to  $30 \pm 3.0$  mm Hg, while rate of oxygen consumption decreased in the tissues studied from 13 to 8.7 mm Hg/min. Thus, there is a decrease in  $pO_2$  level in tissues, and in rate of tissue respiration.

Subsequently, adaptation proceeds as emotional and psychological tension decreases and new motor patterns are developed. In the majority of cases a relative decrease may occur in the external respiration function. As for the possibility of changes in the major metabolic processes in response to weightlessness, the most important processes supporting the major needs of the organism are catabolic and anabolic metabolism.

The absence of continuous gravitational stimulation of catabolic metabolism may lead to a certain amount of deconditioning in the major pathway through which energy is synthesized. This deconditioning may take the form of decreased oxygen utilization in the tissues, decreased coordination of oxidation and phosphorylation in the muscles, and certain changes in and attenuation of aerobic and, possibly, activation of anaerobic, glycolytic processes. Furthermore, participants in 96- and 175-day flights displayed diminished activity of Krebs cycle enzymes (malate dehydrogenase and isocitrate dehydrogenase) and increased accumulation of products of glycolysis, particularly lactate. The accompanying increases in levels of nonesterified fatty acids and triglycerides, along with increases in levels of glucose and pyruvate, attest to a decrease in processes indicative of rate of oxidation. In addition, attention should be devoted to the regulatory role of neuropeptides and changes in the synthesis of secondary messengers (cAMP and cGMP). Not only was the final step in the supply of oxygen molecules to peripheral tissue affected, but products of oxidation were altered both quantitatively and qualitatively with an increase in the less effective glycolytic pathway for synthesizing energy.

Data obtained on the organs, particularly muscles of rats, after 18- to 22-day flights on COSMOS biosatellites, provide convincing and direct proof that the bioenergetics of muscles alter in response to weightlessness. Marked decreases were observed in tissue respiration and oxidative phosphorylation, as well as in coordination between oxidation and phosphorylation. It is to be expected that such fundamental changes in bioenergetics may result in attenuation of the stimuli that help to maintain anabolic metabolism in muscles, the heart, bone tissue, etc., at the required level. In other words, a decrease in bioenergetic stimulation in tissues can disrupt the dynamic equilibrium that exists under normal terrestrial conditions between processes of dissimilation and assimilation of living systems, i.e., one of the most fundamental prerequisites for maintaining a living structure. This may be a causal factor in decrease in muscle mass and performance in weightlessness. It is very significant that the size of the heart decreases and cardiac function may also be attenuated. It is also possible that, without appropriate prophylactic countermeasures, the absence of the muscle exertion required on Earth to overcome the force of gravity would lead not merely to bioenergetic and muscular deconditioning, but also to decreases in periodic need for marked increases in oxygen and oxidation substrate supply and for flushing of metabolic products, associated with exertion on Earth. In other words, the demands on the body's transport systems would decrease. This would first induce functional and then structural deconditioning of the cardiac muscles and vascular bed and would lead to a decrease in total skeletal muscle volume and in mass of the myocardium and associated vasculature. Without doubt, strong emotional or physical stress could lead to various disorders of cardiac functioning, primarily disruption of cardiac rhythm. Thus,

## SPACE BIOLOGY AND MEDICINE

attenuation first of the whole set of catabolic processes, and then of processes of anabolic metabolism and their transport functions, is of particular significance to the pathogenic effects of weightlessness on the body.

Attenuation in weightlessness of the skeletal muscle functions required on Earth to overcome gravity as well as decreases in cardiac function and vascular tonus, lead to weakening of the bioenergetic and structural potential of the body. This is another component of the complex problem of weightlessness effects.

It clearly follows that adherence to a strenuous program of physical training under conditions of weightlessness could significantly diminish disruption of energy and anabolic metabolism in the muscles and avert cardiovascular deconditioning. The set of prophylactic countermeasures, including daily exercise on the bicycle ergometer (approximately 40,000 kgm) and walking on the treadmill for up to 4.33 km per day, along with continual increase in the magnitude of the force exerted on the vertical axis of the body by a belt and bungee cords, and virtually constant wearing (12-16 hours/day) of constant loading suits are intended to substantially eliminate the effects of the lack of gravity. Good results have been obtained on long-term flights, throughout which special attention was devoted to physical exercise.

One more component of the mechanism through which weightlessness effects occur is worthy of consideration. This component is determined by the change in, or more precisely the disruption of, the well-established system of interactions among the sensory organs, the individual's spatial orientation, and, most important, signals from the otolith apparatus. In weightlessness, the otolith apparatus, as well as tactile skin receptors, proprioceptive signals, and interoceptors may tend to produce distorted afferent signals due to elimination of deformation, distension, and pressure on the receptors. This leads to spatial disorientation, the sensation of being upside down or of floating, rotation, etc. These sensations are accompanied by autonomic disturbances, giving rise to facial pallor, vertigo, and sometimes nausea. At the same time fluctuations in blood pressure, pulse and respiration rates, and cold sweating are observed, i.e., marked and clear autonomic disturbance. This pathogenic component of weightlessness effects is important because these autonomic influences on the vascular system, including the vessels of the upper body, coincide with marked changes in the distribution of blood, and in particular with increased perfusion of the vasculature of the head and brain. This circumstance may substantially intensify adverse autonomic effects, which are particularly pronounced during the initial days of exposure to weightlessness and sometimes persist for a longer period.

In developing their conceptual model of the physiological effects of weightlessness, the authors have focussed on the subjective and objective changes that, despite the relatively potent set of prophylactic countermeasures applied, nevertheless have occurred during and especially after long-term space flights.

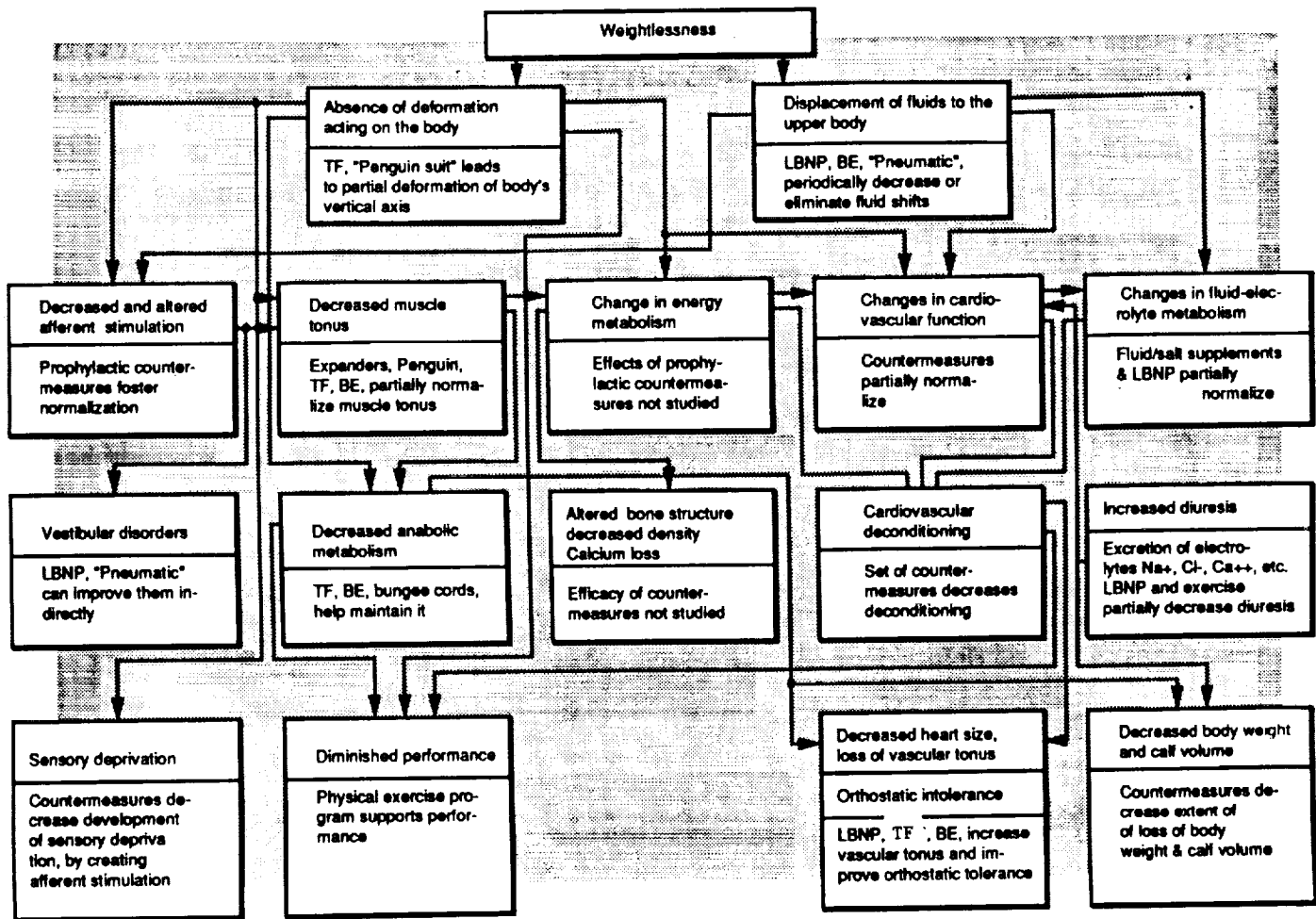
Starting in the first hours of exposure to weightlessness, cosmonauts have developed two major symptoms. First, they have reported the sensation of blood rushing to the head, the duration and severity of which has been subject to individual differences. The majority of cosmonauts have noted nasal congestion, a sensation of pressure in the head, and facial puffiness. The second important subjective symptom during the first day of flight was marked autonomic malaise in the form of frank discomfort and various illusions. It should be emphasized that, despite the experience gained with the entire set of countermeasures, these two pathogenic components of response to weightlessness still have an appreciable effect during long-term flights.

An important aspect of understanding the initial period of exposure to weightlessness, but one which has not yet been studied, is the question of the establishment of clear functional connections between the vestibular apparatus per se and its autonomic components. In this regard, research by I. I. Bryanov and co-workers is of great interest. These authors have

shown that hemodynamic disruptions, accompanied by some degree of microcirculatory disorders at the tissue and intercellular levels, hypertensive shifts, and disruption of fluid-electrolyte metabolism with tissue imbalance of potassium and calcium ions, create conditions conducive to the vestibuloautonomic disorders associated with weightlessness. Under these conditions during space flight, threshold and even subthreshold vestibular stimuli evoked by head and trunk movements are fully capable of giving rise to pronounced responses. Bryanov et al. base their hypothesis on the following argument. It is well-known that there is a connection between hemodynamic status and that of the vestibular system. It is also known that frank vestibular disorders are part of the hypertensive syndrome (set of symptoms occurring when intracranial pressure is elevated) and occur under conditions of engorgement with overfilling of cerebral vessels. Here it should be noted that vestibular nuclei have the most dense vascularization per cubic millimeter of tissue and are extremely sensitive to increases or decreases in circulation. The authors emphasize that in ground-based experiments, subjects are prone to illusions of inverted body position and vertigo, and even waves of nausea, when the head is turned abruptly during the first days of exposure to horizontal or head-down tilt hypokinesia. They associate this with the characteristic hemodynamic changes that attest to increased intracranial pressure and impedance to venous outflow. Evidently a very important role is played here by the increase in blood filling of the vestibular nucleus in the brain. Along with symptoms of venous engorgement and impeded venous outflow, it must also be remembered that the unique pattern of stimulation of the vestibular nuclei occurring under conditions of weightlessness can lead to marked spasms of the cerebral vasculature and possible disruption of cerebral circulation. P.N. Klovskiy and Ye.N. Kosmarskaya noted this linkage between the vestibular nuclei and the nature of blood flow to the brain as early as 1961. In addition, it is well known that phenomena associated with stimulation of the vestibular nuclei occurring in sea and motion sickness induce an overt spasm in the vessels of the carotid artery basin, which is manifested externally through extreme facial pallor. It is reasonable that under these conditions, the effects of the spasm interact with the effects of venous engorgement and moderate cerebral hypoxia. In simulation experiments, when motion sickness is induced in humans, decreased  $pO_2$  in the skin of the face, i.e., in the vascularization basin of the external carotid artery, has been demonstrated directly.

Indirect data suggesting an increase in central venous pressure in participants in all long-term flights are worthy of special attention. On 140- and 175-day flights, venous pressure in the vessels of the calves of cosmonauts (measured using occlusive plethysmography) decreased and was accompanied by diminished tonus of the veins and substantial increase in their compliance. This is worthy of particular attention in connection with the use of lower body negative pressure during space flight, which, given increased compliance and decreased tonus in the veins, may not always be so beneficial. It should be noted that the prophylactic countermeasures applied during long-term (up to 237-326 days) flights essentially eliminated the adverse effects of weightlessness on the cardiovascular system. However, exposure to weightlessness by itself, in its unadulterated form without prophylactic countermeasures, is far from the neutral factor it might seem at first, without a detailed analysis of the information obtained in situations where countermeasures were constantly applied. It is obvious that prophylactic countermeasures, when used on long-term flights (up to 237-326 days), have managed to decrease the adverse effects of weightlessness to a significant extent. However, the authors suggest that despite the extremely positive results and the successes attained, long-term exposure to weightlessness should be evaluated with extreme care. Even very slight changes should be analyzed meticulously, since after short- and long-term flights, a number of physiological changes persist for some time.

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Physiological changes in response to weightlessness and countermeasures on long-term flights: BE - bicycle ergometry; LBNP - lower body negative pressure; TF - training factors

## KEY WORD INDEX

Abiogenesis 18  
Acceleration 14, 82  
Accelerators 71  
Acid Tolerance 67  
Adaptation 1, 4, 11, 16, 65, 74, 78, 86  
Aerobic Capacity 8  
Algae 30, 32  
Algobacterial Cenosis-Fish Ecosystem 30  
Amino Acids 18  
Animals 1  
Anti-g Suit 8  
Aviation Medicine 63  
Barochamber Training 16  
Beetles 74  
Bioenergetics 86  
Biological Effects 20, 71  
Biological Experiments 74  
**Biological Rhythms 1-4, 27, 74**  
Biophysics 71  
Blood Serum 16  
**Body Fluids 6, 78, 86**  
Botany 34, 44  
Brain 58  
Ca<sup>2+</sup> Reactivity 14  
Calcium 60  
Carbohydrate Metabolism 42  
Cardiac Contractility 13  
Cardiac Hypertrophy 11  
**Cardiovascular and Respiratory Systems 4, 8-14, 78, 86**  
Cardiovascular Deconditioning 78  
Catalytic Oxidation 36  
CELSS 30, 32, 34, 82  
*Chlorella* 30, 32  
Circadian Rhythms 1  
Coarctation 13  
Cognitive Task 27  
Cosmic Radiation 71, 74  
Cosmonauts 1, 51, 86  
COSMOS Biosatellites 86  
COSMOS-1667 53, 55  
COSMOS-1887 30, 32, 74, 82  
Countermeasures 48  
Cytology 44, 74  
Decompression Sickness 58  
Deconditioning 86  
Desynchronization 1  
Developmental Biology 74  
Diurnal Variations 27  
*Drosophila melanogaster* 74  
Drugs 8, 38, 78  
*E. coli* 74  
Endocrinology 4, 13, 86  
**Enzymology 15-16, 42, 86**  
Equipment and Instrumentation 28, 82  
Erythrocytes 67  
Exercise Loading 8

## KEY WORD INDEX

**Exobiology** 18-20  
Extracellular Fluid 6  
Female 13  
Fibrogenesis 20  
Fish 30  
Gastrointestinal System 78  
Genetics 74  
Glycolysis 42  
Guppies 74  
Hadrons 71  
*Haplopappus* 74  
Hematology 67, 78  
Hemodynamics, Central and Peripheral 10  
High Altitude Hypoxia 11  
**Histology** 24, 44  
**Human Performance** 4, 25-28, 63, 65, 82  
Humans 1, 6, 8, 10, 25, 27, 28, 38, 48, 51, 59, 63, 65, 78, 86  
Hydration 6  
Hydrogen Peroxide 36  
Hypergravity 14  
Hypertension 10  
Hypodynamia 82  
Hypokinesia 15, 42, 60, 62, 82  
    with Head-down Tilt 6, 8, 25, 38, 48, 78  
Hypoxia 16, 24, 68, 70  
Immersion 25  
Immersion, Dry 10  
Immobilization 13  
Immobilization Cages 62  
Immobilization Stress 42  
Immunology 78, 82  
Ionizing Radiation 44, 68, 70  
Karkas Suit 78  
LBNP 78, 86  
**Life Support Systems** 30- 36, 82  
Lithosphere 18  
Liver 68, 70  
Low Temperature 36  
Lungs 16  
*Macaca mulatta* 74  
Magnetic Field 67  
Males 1, 10, 14, 16, 42, 50, 55, 59, 60, 62, 67, 68, 70, 78  
Mathematical Modeling 2  
Matter Balance 36  
**Metabolism** 11, 38-42, 60, 62, 78, 82, 86  
    Metabolism Cell 74  
    Metabolism Mineral, Fats 6  
    Metabolism, Fat, Carbohydrates 4  
**Microbiology** 30, 32, 34, 44, 74  
Microwave Radiation 68, 70  
Mineral Density 48  
Mitochondria 15  
Monkeys 53  
Morphology 55  
Motion Sickness 82  
**Musculoskeletal System** 15, 48 - 51, 78, 82, 86  
**Neurophysiology** 28, 53- 59, 82, 86  
Nitrogen 38

## KEY WORD INDEX

Nucleic Acids 11  
**Nutrition** 60-62, 82  
One-Celled Organisms 44  
Operational Medicine 82  
Operators 25, 27, 28  
Orthostatic Intolerance 8  
Orthostatic Loading 59  
Orthostatic Tolerance 10  
Oxidative Enzymes 15  
Pathogenesis 58, 86  
Patients 10  
Peptide Hydrolases 16  
**Perception** 63  
Periodic Structure 2  
Periodontium 50  
Physical Exercise 6, 8, 38, 48, 78, 86  
Pilot Training 63  
Pilots 63  
Plant and Animal Cells 44  
Population Studies 74  
Precellular Organisms 44  
Prophylactic Countermeasures 6, 8, 38, 50, 78, 82, 86  
Proprioception 25  
Proteolysis 16  
Provocative Tests 8  
**Psychology** 28, 63, 65, 82  
Rabbits 11, 58  
**Radiobiology** 44, 67- 71, 74, 82  
Radioprotective Effects 68, 70  
Raster Method 2  
Rats 13, 14, 15, 16, 24, 42, 50, 51, 55, 60, 62, 67, 68, 70, 86  
Receptor Organs 55  
Recovery Period 15  
Research Apparatus 28  
Research Methods 28  
Salyut 86  
Sensorimotor Performance 25  
Serum Proteins 38  
Shift Work 4, 27  
Silicon 50  
Simulation 18  
Skeletal Bones 48  
Skeletal Muscles 15  
Skeletal System 51  
Skin Basophils 24  
Sleep 53, 82  
Soyuz 86  
**Space Biology and Medicine** 74- 86  
Space Flight 1, 4, 30, 32, 44, 51, 53, 55, 74, 82, 86  
    Space Flight, Manned 34  
Space Motion Sickness 86  
Spatial Orientation 63  
Stand Test 59  
Stick Insects 74  
Stress 4, 13, 65, 82  
Tail Suspension 50, 60  
*Tetrahymena pyriformis* 74  
Thermal Polycondensation 18



Thiamine 62  
Thyroid 4  
Thyroid Hormones 13  
Tilt Test 18, 0, 59  
Tissue Cultures 44  
Tissue Respiration 16  
Tortoises 51  
Tritons 74  
Ultraviolet Therapy 6  
Vegetable Protein 60  
Ventricular Actomyosin 14  
Vestibular Activity 59  
Vestibular System 55  
Vitamin Deficiency 62  
Volcanic Activity 18  
Water Regeneration 36  
Weightlessness 82, 86  
Weightlessness Simulations 86  
Wheat 34  
*Wolffia* 74  
Work Schedules 1



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